## 10/724,638

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FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS' ENTERED AT 14:28:55 ON 24 FEB 2006
L1
       22922 S IFOSFAMIDE
L2
        194908 S CYCLOPHOSPHAMIDE
         55323 S CYCLODEXTRIN
L3
           77 S L3 AND (L1 OR L2)
L4
            54 DUP REM L4 (23 DUPLICATES REMOVED)
L5
         53333 S HYDROXYPROPYL
L6
         53061 S HP OR HPCD OR HPBCD
L7
         72327 S NEPHROTOXIC?
L8
L9
         1202 S NEPHROPROTECT?
L10
       6279353 S REDUC?
       3541621 S LOWER?
L11
L12
       5300213 S DECREAS?
            23 S L5 AND (L6 OR L7 OR L8 OR L9 OR L10 OR L11 OR L12)
L13
            31 S L5 NOT L13
L14
=> S ACROLEIN
L15
       21700 ACROLEIN
=> S L3 AND (L15 OR L9)
            6 L3 AND (L15 OR L9)
L16
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L13 ANSWER 1 OF 23 MEDLINE on STN ACCESSION NUMBER: 96203727 MEDLINE DOCUMENT NUMBER: PubMed ID: 8616908

Comparison of several antiangiogenic regimens alone and TITLE:

with cytotoxic therapies in the Lewis lung carcinoma. Teicher B A; Holden S A; Ara G; Korbut T; Menon K

AUTHOR: CORPORATE SOURCE: Dana-Farber Cancer Institute, Boston, MA 02115, USA.

CONTRACT NUMBER: PO1-CA19589 (NCI)

PO1-CA31303 (NCI) RO1-CA50174 (NCI)

Cancer chemotherapy and pharmacology, (1996) 38 (2) 169-77. SOURCE:

Journal code: 7806519. ISSN: 0344-5704. GERMANY: Germany, Federal Republic of Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

PUB. COUNTRY:

DOCUMENT TYPE:

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199606

ENTRY DATE: Entered STN: 19960620

Last Updated on STN: 19970203 Entered Medline: 19960611

The efficacy of several potential antiangiogenic agents, TNP-470, minocycline, suramin, genistein, interferon delta 4, 14(sulfated)-betacyclodextrin and tetrahydrocortisol, alone and in combination with cytotoxic therapies was examined against primary and metastatic Lewis lung carcinoma. The antiangiogenic agents when administered as single agents or in two-agent combinations were only modestly active as antitumor Three antiangiogenic agent combinations, TNP-470/minocycline, TNP-470/14(SO4)beta-CD/THC and minocycline/14(SO4)beta-CD/THC, produced significant increases in tumor growth delay and decreases in the number of lung metastases when administered along with cyclophosphamide compared with cyclophosphamide alone. Two antiangiogenic agent combinations, minocycline/interferon delta 4 and minocycline/14(SO4)beta-CD/THC, produced significant decreases in the number of lung metastases when administered alone with adriamycin compared with adriamycin alone. The antiangiogenic combinations of TNP-470/minocycline, TNP-470/suramin, TNP-470/genistein, TNP-470/interferon delta 4 and TNP-470/14(SO4)beta-CD/THC, resulted in increased tumor growth delays when administered along with CDDP, BCNU, fractionated radiation or 5-fluorouracil. There was not always a direct correlation between the antiangiogenic regimen that was most beneficial against the primary tumor as compared with disease metastatic to the lungs. These studies establish that a broad range of antiangilogenic therapies can interact in a positive manner with cytotoxic therapies.

L13 ANSWER 2 OF 23 MEDLINE on STN 96073730 ACCESSION NUMBER: MEDLINE PubMed ID: 8535401 DOCUMENT NUMBER:

Increase in total blood leukocyte count following TITLE:

intranasal administration of recombinant human granulocyte

colony-stimulating factor (rhG-CSF) in rabbits with

cyclophosphamide-induced leukopenia.

Watanabe Y; Kikuchi R; Kiriyama M; Nakagawa K; Oe J; Nomura AUTHOR:

H; Maruyama K; Matsumoto M

CORPORATE SOURCE: Department of Pharmaceutics, Showa College of

Pharmaceutical Sciences, Tokyo, Japan.

SOURCE: Biological & pharmaceutical bulletin, (1995 Aug) 18 (8)

1084-8.

Journal code: 9311984. ISSN: 0918-6158.

PUB. COUNTRY: Japan

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH:

ENTRY DATE: Entered STN: 19960221

Last Updated on STN: 19960221 Entered Medline: 19960205

We investigated the effects of intranasal (i.n.) administration of recombinant human granulocyte colony-stimulating factors (rhG-CSF) on the total count of leukocytes in peripheral blood (total blood leukocyte count) of rabbits with leukopenia who received cyclophosphamide (CPA). When CPA (30 mg/kg per d) was administered intravenously, the total blood leukocyte count decreased to levels below 5000/microliters approximately 4 d after the initiation of CPA multiple dosing. The decreased level of the total blood leukocyte count was maintained throughout the period of CPA dosing. RhG-CSF was given

once a day for 3 d in CPA-treated rabbits via i.n. administration of aqueous preparations containing rhG-CSF with or without alpha-cyclodextrin (alpha-CyD). The total blood leukocyte count increased from levels below 5000/microliters to the normal physiological level following i.n. administration of rhG-CSF preparation and reduced the period of leukopenia induced by CPA. The coadministration of rhG-CSF and alpha-CyD was more effective in increasing the total blood leukocyte count. It is suggested that i.n. administration of rhG-CSF is promising for reducing the risk of cytotoxic chemotherapy (CPA)-induced leukopenia as an adverse side effect.

L13 ANSWER 3 OF 23 MEDLINE ON STN
ACCESSION NUMBER: 94127827 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7507654

TITLE: Response of the FSaII fibrosarcoma to antiangiogenic

modulators plus cytotoxic agents.

AUTHOR: Teicher B A; Holden S A; Ara G; Northey D CORPORATE SOURCE: Dana-Farber Cancer Institute, Boston, MA 02115.

CONTRACT NUMBER: PO1-CA19589 (NCI)

PO1-CA38493 (NCI)

SOURCE: Anticancer research, (1993 Nov-Dec) 13 (6A) 2101-6.

Journal code: 8102988. ISSN: 0250-7005.

PUB. COUNTRY: Greece

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199402

ENTRY DATE: Entered STN: 19940314

Last Updated on STN: 19970203 Entered Medline: 19940228

The formation of a blood supply (angiogenesis) is critical to the growth AR of solid tumors. The naturally occurring steroid tetrahydrocortisol, the synthetic cyclodextrin derivative beta-cyclodextrin tetradecasulfate, and the tetracycline derivative minocycline have antiangiogenic activity. Tetrahydrocortisol (125 mg/kg) and betacyclodextrin tetradecasulfate (1000 mg/kg) in a 1:1 molar ratio by continuous infusion over 14 days and minocycline (10 mg/kg) administered i.p. daily from day 4 to day 18 postimplantation of the FSaII fibrosarcoma did not alter the growth of the tumor. These antiangiogenic modulators were not cytotoxic toward FSaIIC tumor cells or bone marrow CFU-GM when tumor-bearing animals were treated and cytotoxicity determined by colony formation in culture. The antiangiogenic modulators markedly increased the cytotoxicity of cyclophosphamide toward FSaIIC tumor cells and to a much lesser degree toward bone marrow CFU-GM. The cytotoxicity of CDDP and radiation was enhanced only by administration of the three modulators in combination. In tumor growth delay studies, the three modulator combination increased the effectiveness of CDDP by 1.5-fold, of cyclophosphamide by 1.9-fold and of radiation by 1.4-fold. Although the antiangiogenic therapies alone did not substantially reduce the number of lung metastases compared with the untreated controls, addition of the antiangiogenic agents to treatment with the cytotoxic therapies reduced not only the number of lung metastases formed from the primary tumor but also reduced the number of large metastases. Thus, antiangiogenic therapies can potentiate the efficacy of standard anticancer therapies.

L13 ANSWER 4 OF 23 MEDLINE ON STN
ACCESSION NUMBER: 94094423 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8269604

TITLE: beta-cyclodextrin tetradecasulfate/tetrahydrocort

isol +/- minocycline as modulators of cancer therapies in vitro and in vivo against primary and metastatic Lewis lung

carcinoma.

AUTHOR: Teicher B A; Sotomayor E A; Huang Z D; Ara G; Holden S;

Khandekar V; Chen Y N

CORPORATE SOURCE: Dana-Farber Cancer Institute, Boston, MA 02115.

CONTRACT NUMBER: PO1-CA38493 (NCI)

SOURCE: Cancer chemotherapy and pharmacology, (1993) 33 (3) 229-38.

Journal code: 7806519. ISSN: 0344-5704. GERMANY: Germany, Federal Republic of Journal; Article; (JOURNAL ARTICLE)

DOCUMENT TYPE: Journal; LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199402

PUB. COUNTRY:

ENTRY DATE: Entered STN: 19940215

Last Updated on STN: 19970203

## Entered Medline: 19940201

Tetrahydrocortisol, beta-cyclodextrin tetradecasulfate, and minocycline used alone or in combination are not very cytotoxic toward EMT-6 mouse mammary tumor cells growing in monolayer. Tetrahydrocortisol (100 microM, 24 h) and beta-cyclodextrin tetradecasulfate (100 microM, 24 h) protected EMT-6 cells from the cytotoxicity of CDDP, melphalan, 4-hydroperoxycyclophosphamide, BCNU, and X-rays under various conditions of oxygenation and pH. Minocycline (100 microM, 24 h) either had no effect upon or was additive with the antitumor alkylating agents or X-rays in cytotoxic activity toward the EMT-6 cells in culture. The combination of the three modulators either had no effect upon or was to a small degree protective against the cytotoxicity of the antitumor alkylating agents or X-rays. The Lewis lung carcinoma was chosen for primary tumor growth-delay studies and tumor lung-metastases studied. Tetrahydrocortisol and beta-cyclodextrin tetradecasulfate were given in a 1:1 molar ratio by continuous infusion over 14 days, and minocycline was given i.p. over 14 days, from day 4 to day 18 post tumor implantation. The combination of tetrahydrocortisol/betacyclodextrin tetradecasulfate diminished the tumor growth delay induced by CDDP and melphalan and produced modest increases in the tumor growth delay produced by **cyclophosphamide** and radiation.

Minocycline co-treatment increased the tumor growth delay produced by CDDP, melphalan, radiation, bleomycin, and, especially cyclophosphamide, where 4 of 12 animals receiving minocycline (14 x = 5 mg/kg, days 4-18) and cyclophosphamide (3 x 150 mg/kg, days 7, 9, 11) were long-term survivors. The 3 modulators given in combination produced further increases in tumor growth delay with all of the cytotoxic therapies, and 5 of 12 of the animals treated with the 3-modulator combination and cyclophosphamide were long-term survivors. Although neither tetrahydrocortisol/beta-cyclodextrin tetradecasulfate, minocycline, nor the three modulator combination impacted the number of lung metastases, there was a decrease in the number of large lung metastases. Treatment with the cytotoxic therapies alone **reduced** the number of lung metastases. Addition of the modulators to treatment with the cytotoxic therapies resulted in a further **reduction** in the number of lung metastases. These results indicate that agents that inhibit the breakdown of the extracellular matrix can be useful additions to the treatment of solid tumors.

L13 ANSWER 5 OF 23 MEDLINE on STN
ACCESSION NUMBER: 93046201 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1384969

TITLE: Antiangiogenic agents potentiate cytotoxic cancer therapies

against primary and metastatic disease. Teicher B A; Sotomayor E A; Huang Z D

AUTHOR: Teicher B A; Sotomayor E A; Huang Z D
CORPORATE SOURCE: Dana-Farber Cancer Institute, Boston, Mas

CORPORATE SOURCE: Dana-Farber Cancer Institute, Boston, Massachusetts 02115.

CONTRACT NUMBER: PO1-CA38493 (NCI)

SOURCE: Cancer research, (1992 Dec 1) 52 (23) 6702-4.

Journal code: 2984705R. ISSN: 0008-5472.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199212

ENTRY DATE: Entered STN: 19930122

Last Updated on STN: 19970203 Entered Medline: 19921216

The formation of a blood supply (angiogenesis) is critical to the growth of solid tumors. The naturally occurring steroid tetrahydrocortisol, the synthetic cyclodextrin derivative beta-cyclodextrin tetradecasulfate, and the tetracycline derivative minocycline have antiangiogenic activity. Tetrahydrocortisol and beta-cyclodextrin tetradecasulfate in a 1:1 molar ratio by continuous infusion over 14 days and minocycline administered i.p. over 14 days from day 4 to day 18 postimplantation of the Lewis lung carcinoma significantly increased the growth delay of the primary tumor after treatment with cis-diamminedichloroplatinum(II), melphalan, cyclophosphamide, Adriamycin, bleomycin, and radiation therapy administered in standard regimens. Addition of the antiangiogenic agents to treatment with the cytotoxic therapies not only reduced the number of lung metastases formed from the primary tumor but also **reduced** the number of large metastases. Five of 12 animals treated with the antiangiogenic modulators and cyclophosphamide were long-term survivors (> 120 days). Thus, antiangiogenic therapies can potentiate the efficacy of standard anticancer therapies.

L13 ANSWER 6 OF 23 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:568991 BIOSIS PREV200300567947 DOCUMENT NUMBER:

Efficacy of posaconazole in a murine model of CNS TITLE:

aspergillosis.

Imai, J. [Reprint Author]; Singh, G. [Reprint Author]; AUTHOR (S):

Clemons, K. V. [Reprint Author]; Stevens, D. A. [Reprint

Authorl

CORPORATE SOURCE: Calif. Inst. Med. Res., San Jose, CA, USA

SOURCE:

Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2003) Vol. 43, pp. 432. print. Meeting Info.: 43rd Annual Interscience Conference on Antimicrobial Agents and Chemotherapy. Chicago, IL, USA. September 14-17, 2003. American Society for Microbiology.

Conference; (Meeting) DOCUMENT TYPE:

Conference; Abstract; (Meeting Abstract)

LANGUAGE: ENTRY DATE:

English

Entered STN: 3 Dec 2003

Last Updated on STN: 3 Dec 2003

Background: Human CNS infection with Aspergillus fumigatus, despite therapy, has >90% mortality. We compared the efficacies of posaconazole (POS), amphotericin B (AmB), itraconazole (ICZ) and caspofungin (CF) for treatment potential. Methods: Male CD-1 mice were immunosuppressed with cyclophosphamide (200 mg/kg, i.p.), 2 days prior to, and every 5 days after infection. Mice were infected intracerebrally with 7.05X106 conidia/mouse of A. fumigatus. Groups of mice (n=10) were given AmB at 3 mg/kg (i.p., QD), POS in sterile water at 5, 25 or 100 mg/kg (PO, QD), CF at 5 mg/kg (i.p., QD), or ICZ in 34% cyclodextrin (HPbetaCD) at 50 mg/kg (PO, BID). Diluent controls received HPbetaCD (PO, BID) or 5% D5W (i.p. QD). Therapy began 1 day after infection for 10 days. On day 14, fungal burdens were determined in survivors by plating of brain and kidney homogenates. Results: Mice treated with HPbetaCD had 100% mortality and gtoreq80% given D5W or ICZ died, whereas CF, AmB, and POS (all doses) had 40, 70 and gtoreq90% survival, respectively. Treatment with AmB, or POS at 5, 25, or 100 mg/kg significantly prolonged survival over mice given HPbetaCD (Pltoreq0.0001), D5W (Pltoreq0.02), or those given ICZ (Pltoreq0.01). All POS regimens were superior in prolonging survival over CF (Pltoreq0.02). AmB, and POS at 5, 25, or 100 mg/kg were superior to D5W (Pltoreq0.02), CF (Pltoreq0.04), and ICZ (Pltoreq0.009) in reducing CFU from both the brain and the kidneys. AmB and POS were also equivalent to each other in prolonging survival (P>0.05) or reducing CFU in either organ. No animals were cured of infection in either organ by any treatment regimen. Conclusions: POS at 5, 25, or 100 mg/kg showed no overt toxicity and was superior in prolonging survival and reducing CFU .when compared to control groups, CF, or ICZ; all regimens of POS were equivalent to AmB for survival and CFU. However, POS in this vehicle did not show dose responsiveness in CFU reduction or effect cure. Overall, POS shows promising efficacy for the treatment of CNS aspergillosis.

L13 ANSWER 7 OF 23 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:499322 BIOSIS

DOCUMENT NUMBER: PREV200200499322

Pharmacokinetics of a 14 day course of itraconazole TITLE: nanocrystals given intravenously to allogeneic

haematopoietic stem cell transplant (HSCT) recipients.

AUTHOR(S):

Donnelly, J. P. [Reprint author]; Mouton, J. W.; Blijlevens, N. M. A. [Reprint author]; Smiets, A. [Reprint author]; Verweij, P. E. [Reprint author]; de Pauw, B. E.

[Reprint author]

CORPORATE SOURCE: UMC St Radboud, Nijmegen, Netherlands

SOURCE: Abstracts of the Interscience Conference on Antimicrobial

Agents and Chemotherapy, (2001) Vol. 41, pp. 5. print. Meeting Info.: 41st Annual Meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy.

Chicago, Illinois, USA. September 22-25, 2001.

DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

Conference; (Meeting Poster)

LANGUAGE: English

Entered STN: 25 Sep 2002 ENTRY DATE:

Last Updated on STN: 25 Sep 2002

AB Background: A new nanocrystal formulation of itraconazole is thought safer than hydroxy-beta-cyclodextrin for treating patients receiving ciclosporin (CSA). We studied the pharmacokinetics of ITR-NC in a

homogeneous cohort of 6 adults receiving an allogeneic matched-related HSCT who tolerate oral drugs poorly. Methods: After giving informed consent, all patients were managed with a triple lumen IV catheter, given idarubicin, cyclophosphamide and TBI for conditioning therapy, and the same antimicrobial prophylaxis. On days -6 and -5 preHSCT 200 mg ITR-NC was given IV q12h followed by 200 mg q24 for the next 12 days. CS/ 3 mg/kg/d was started on d-1 HSCT (d+6 of IT-NC). Plasma was obtained at 0, 2, 12, 14, 24, 26, 36, 38, 48, 50, 72, 74, 96, 98, 120, 122, 144, 144.25, 144.5, 145, 146, 146.5,, 147, 148, 150, 152, 156, 160, 168,, 216,, 264,, 312, 312.25, 312.5, 313, 314, 314.5, 315, 316, 318, 320, 324,, 328, 336, 360, 384, 408, 432, 648 h after the first dose. A 2-compartment open model and non-compartmental analysis were done using Winnonlin. Results: The mean+-SD Vss=1677+-827 L, AUC24=51558+-10635 mug.h/L, Cmax=5084+-2209, Cl=3.35+-1.8 L/h and terminal t1/2=346+-225 h. Steady state was not reached and \*500 mug/L was maintained in 5 cases for at least 9 days after stopping treatment. 5 patients had minor complaints about the drug of which 2 had transient hypotension. CSA was reduced by 23-33% in 4 cases (1 fluid retention), stopped in 1 (fluid retention) and not adjusted in 1 (fluid retention and neurotoxicity). Conclusions: IT-NC was well tolerated. A 14 day-course provides \*500 mug/L for 3 weeks but the dosage of CSA should be reduced by a third to forestall toxicity.

L13 ANSWER 8 OF 23 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004221744 EMBASE

Guidelines for the use of antifungal agents in the TITLE:

treatment of invasive Candida and mould infections. AUTHOR: Slavin M.A.; Szer J.; Grigg A.P.; Roberts A.W.; Seymour

J.F.; Sasadeusz J.; Thursky K.; Chen S.C.; Morrissey C.O.;

Heath C.H.; Sorrell T.

CORPORATE SOURCE: M.A. Slavin, Vic. Infectious Diseases Service, Royal

Melbourne Hospital, Grattan Street, Melbourne, Vic. 3050.

monica.slavin@mh.org.au

Internal Medicine Journal, (2004) Vol. 34, No. 4, pp. SOURCE:

192-200. Refs: 46

ISSN: 1444-0903 CODEN: IMJNAK

Australia

COUNTRY:

DOCUMENT TYPE: Journal; General Review FILE SEGMENT: Internal Medicine

030 Pharmacology

037 Drug Literature Index 038 Adverse Reactions Titles

039 Pharmacy

English LANGUAGE: SUMMARY LANGUAGE: English

Entered STN: 20040610 ENTRY DATE:

Last Updated on STN: 20040610

Treatment of invasive fungal infections is increasingly complex. Amphotericin B deoxycholate has long been the mainstay of treatment. However, there has been increasing recognition of both the propensity for nephrotoxicity in haematology, transplant and intensive care patients as well as its adverse impact on morbidity and mortality. This has coincided with the availabilty of newer, and in certain settings, more effective antifungal agents. Although the newer agents clearly cause less nephrotoxicity than amphotericin B, drug interactions, hepatic effects and unique side-effects need to be considered. The spectrum of the newer triazoles and echinocandins varies, highlighting the importance of accurate identification of the causative organism where possible. Consensus Australian quidelines have been developed to assist clinicians with treatment choices by reviewing the current evidence for the efficacy, the toxicity and the cost of these agents.

L13 ANSWER 9 OF 23 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights

reserved on STN

ACCESSION NUMBER: 94196366 EMBASE

DOCUMENT NUMBER: 1994196366

Interaction of taxol and other anticancer drugs with TITLE:

hydroxypropyl-β- cyclodextrin.

AUTHOR: Cserhati T.; Hollo J.

CORPORATE SOURCE: Central Research Inst. for Chemistry, Hungarian Academy of

Sciences, PO Box 17,1525 Budapest, Hungary

International Journal of Pharmaceutics, (1994) Vol. 108, SOURCE:

No. 1, pp. 69-75.

ISSN: 0378-5173 CODEN: IJPHDE

COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 037 Drug Literature Index

LANGUAGE: English SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 940803

Last Updated on STN: 940803

AB The interaction between 23 anticancer drugs and hydroxypropyl
-β- cyclodextrin (HP.beta.CD) was studied by
reversed-phase charge-transfer thin-layer chromatography and the relative
strength of interaction was calculated. HP.beta.CD formed
inclusion complexes with 15 compounds, the complex always being more
hydrophilic than the uncomplexed drug. The inclusion forming capacity of
drugs differed considerably according to their chemical structure. The
intensity of interaction significantly increased with increasing
hydrophobicity of the guest molecule, demonstrating the preponderant role
of hydrophobic interactions in inclusion complex formation.

L13 ANSWER 10 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1354741 CAPLUS

DOCUMENT NUMBER: 144:94351

TITLE: A method of improving treatments in rheumatic and

arthritic diseases using strontium salts

INVENTOR(S): Christgau, Stephan; Hansen, Christian; Nilsson, Henrik

PATENT ASSIGNEE(S): Osteologix A/S, Den.
SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.					KIND		DATE		APPLICATION NO.						DATE				
						-													
WO	2005	1231	93		A2		2005	1229	1	NO 2	005-1	DK40	4		20	00506	517		
	W:	ΑE,	AG,	AL,	ΑM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	B₩,	BY,	ΒZ,	CA,	CH,		
		CN,	co,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,		
		GE,	GH,	GM,	HR,	ΗU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	ΚM,	ΚP,	KR,	ΚZ,		
		LC,	LK,	LR,	LS,	LT,	LU,	LV,	ΜA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NA,		
	NG, NI, NO			NO,	ΝZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,		
		SL,	SM,	SY,	ТJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,		
		ZA,	ZM,	ZW															
	RW:	BW,	GH,	GM,	ΚE,	LS,	MW,	ΜZ,	NA,	SD,	SL,	SZ,	ΤZ,	UG,	ZM,	ZW,	ΑM,		
		ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,		
		EE,	ES,	FΙ,	FR,	GB,	GR,	ΗU,	ΙE,	IS,	ΙT,	LT,	LU,	MC,	NL,	PL,	PT,		
		RO,	SE,	SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,		
		MR,	ΝE,	SN,	TD,	TG													
DRITY	RITY APPLN. INFO.:									DK 2004-950					A 20040617				

PRIO Improved treatments of joint diseases, such as, e.g. osteoarthritis and rheumatoid arthritis, and pain, comprise a strontium-containing compound administered alone or in combination with one or more second therapeutically and/or prophylactically active substances. The second active substance is selected from the group consisting of bisphosphonates, glucosamine, pallitative agents, analgesic agents, disease modifying anti-rheumatic compds. (DMARDs), selective estrogen receptor modulators (SERMs), aromatase inhibitors, non-steroidal anti-inflammatory agents (NSAIDs), COX-2 inhibitors, COX-3 inhibitors, opioids, inhibitors/antagonists of IL-1, inhibitors/antagonists of TNF-α, inhibitors of matrix metallo-proteinases (MMPs), cathepsin K inhibitors, inhibitors/antagonists of RANK-ligand, statins, glucocorticoids, chondroitin sulfate, NMDA receptor antagonists, inhibitors of interleukin-I converting enzyme, Calcitonin gene related peptide antagonists, glycine antagonists, vanilloid receptor antagonists, inhibitors of inducible nitric oxide synthetase (iNOS), N-acetylcholine receptor agonists, neurokinin antagonists, neuroleptic agents, PAR2 receptor antagonists and anabolic growth factors acting on joint tissue components. Pharmaceutical compns. comprising a strontium-containing compound and a second therapeutically and/or prophylactically active substance as defined above are also described. Thus, a tablet formulation to be administrated one to two times daily contained alendronate 10 mg, strontium malonate 200 mg, lactose 100 mg, corn starch (for mixing) 15 mg, corn starch (for paste) 15 mg, and magnesium stearate 10 mg.

L13 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:411062 CAPLUS

DOCUMENT NUMBER: 142:442337

TITLE: Therapeutic use of androgens for various conditions

including cardiovascular disease, immune disorders,

trauma, and inflammation

INVENTOR(S):

Reading, Christopher L.; Ahlem, Clarence N.; Auci, Dominick L.; Dowding, Charles; Frincke, James M.; Li, Mei; Page, Theodore M.; Stickney, Dwight R.; Trauger,

Richard J.; White, Steven K.

PATENT ASSIGNEE(S):

U.S. Pat. Appl. Publ., 180 pp., Cont.-in-part of U.S. SOURCE:

Ser. No. 651,515. CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English'

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
				_	
US 2005101581	A1	20050512	US 2003-728400		20031205
US 2004138187	A1	20040715	US 2003-651515		20030828
PRIORITY APPLN. INFO.:			US 2002-407146P	Ρ	20020828
			US 2002-408332P	P	20020904
			US 2003-479257P	P	20030617
			US 2003-651515	A2	20030828

MARPAT 142:442337 OTHER SOURCE(S):

The invention relates to the use of compds. to ameliorate or treat  $\boldsymbol{a}$ condition such as a cystic fibrosis, neutropenia or other exemplified conditions including cardiovascular disease, immune disorders, trauma, and inflammation. Exemplary compds. that can be used include  $3\beta$ -hydroxy-17 $\beta$ -aminoandrost-5-ene,  $3\beta$ -hydroxy-16 $\alpha$ fluoro-17β-aminoandrost-5-ene, 3α-hydroxy-16α-fluoro- $17\beta$ -aminoandrost-5-ene,  $3\beta$ -hydroxy- $16\beta$ -fluoro- $17\beta$ -aminoandrost-5-ene,  $1\alpha$ ,  $3\beta$ -dihydroxy- $4\alpha$ -fluoroandrost-5-ene-17-one,  $1\alpha$ ,  $3\beta$ ,  $17\beta$ -trihydroxy- $4\alpha$ -fluorandrost-5ene,  $1\beta$ ,  $3\beta$ -dihydroxy- $6\alpha$ -bromoandrost-5-ene,  $1\alpha$ -fluoro-3 $\beta$ ,  $12\alpha$ -dihydroxyandrost-5-ene-17-one,  $1\alpha$ -fluoro- $3\beta$ ,  $4\alpha$ -dihydroxyandrost-5-ene and

L13 ANSWER 12 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

 $4\alpha$ -fluoro- $3\beta$ ,  $6\alpha$ ,  $17\beta$ -trihydroxyandrostane.

2004:780351 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

141:266004

TITLE: Aqueous Ifosfamide compositions for

parenteral administration and a process for their

preparations

Daftary, Gautam Vinod; Pai, Srikanth Annappa; INVENTOR(S):

Rivankar, Sangeeta Hanurmesh; Subbappa, Praveen Kumar

PATENT ASSIGNEE(S): Bharats Serums & Vaccines Ltd., India

U.S. Pat. Appl. Publ., 10 pp. SOURCE:

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004186074	A1	20040923	US 2003-724638		20031202
PRIORITY APPLN. INFO.:			IN 2002-MU758	Α	20021202
AB The present inventi	on pro	vides aqueous	Ifosfamide compns	and	a

process for their preparation, in which the compns. have a reduced toxicity over and above the concomitant use of the uroprotective agent, Mesna. Aqueous Ifosfamide compns. can be prepared at concns. as high has 1,1000 mg/mL.

L13 ANSWER 13 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:490697 CAPLUS

DOCUMENT NUMBER: 141:42928

Ifosfamide compositions for parenteral TITLE:

administration and a process for their preparation

INVENTOR(S): Daftary, Gautam Vinod; Pai, Srikanth Annappa;

Rivankar, Sangeeta Hanurmesh; Praveen, Kumar Subbappa

PATENT ASSIGNEE(S): Bharat Serums and Vaccines Ltd., India

PCT Int. Appl., 31 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent

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LANGUAGE:
                         English
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PATENT INFORMATION:

FAMILY ACC. NUM. COUNT:

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KIND
       PATENT NO.
                                                   DATE
                                                                     APPLICATION NO.
                                                                                                             DATE
                                        ____
                                                    -----
       WO 2004050012
                                        A2
                                                   20040617
                                                                      WO 2003-IN376
                                                                                                             20031202
                                         A3
                                                   20041021
       WO 2004050012
              W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
                    CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
                    LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
              RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
                    ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG AB AB 20040617 CA 2003–2507848 20031202 A2 20050907 EP 2003–808347 20031202
       CA 2507848
       EP 1569663
             R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
       BR 2003016968
                                                   20051025
                                                                       BR 2003-16968
                                                                                                             20031202
                                         Α
PRIORITY APPLN. INFO.:
                                                                       IN 2002-MU785
                                                                                                        A 20021202
                                                                       WO 2003-IN376
```

The present invention provides aqueous Ifosfamide compns. and a process for their preparation, in which the compns. have a reduced toxicity over and above the concomitant use of the uroprotective agent, Mesna. Aqueous compns. of **Ifosfamide** can be prepared at a concentration as high as 1100 mg/mL.

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L13 ANSWER 14 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
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ACCESSION NUMBER:

INVENTOR(S):

DOCUMENT NUMBER:

TITLE:

2004:203677 CAPLUS 140:229914

Immunostimulatory methods and compositions with androgen derivatives and other therapeutic uses Reading, Christopher; Ahlem, Clarence N.; Auci,

Dominick L.; Dowding, Charles; Frincke, James; Li, Mei; Page, Theodore M.; Trauger, Richard J.; Stickney, Dwight R.; White, Steven K.

Hollis-Eden Pharmaceuticals, Inc., USA

PATENT ASSIGNEE(S): SOURCE:

PCT Int. Appl., 380 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE			
WO 2004019953	A1 20040311	WO 2003-US327186	20030828			
W: AE, AG, AL	, AM, AT, AU, A2,	BA, BB, BG, BR, BY,	BZ, CA, CH, CN,			
CO, CR, CU	, CZ, DE, DK, DM,	DZ, EC, EE, ES, FI,	GB, GD, GE, GH,			
GM, HR, HU	, ID, IL, IN, IS,	JP, KE, KG, KP, KR,	KZ, LC, LK, LR,			
LS, LT, LU	, LV, MA, MD, MG,	MK, MN, MW, MX, MZ,	NO, NZ, OM, PH,			
PL, PT, RO	, RU, SD, SE, SG,	SK, SL, TJ, TM, TN,	TR, TT, TZ, UA,			
UG, US, UZ	, VC, VN, YU, ZA,	ZM, ZW				
RW: GH, GM, KE	, LS, MW, MZ, SD,	SL, SZ, TZ, UG, ZM,	ZW, AM, AZ, BY,			
KG, KZ, MD	, RU, TJ, TM, AT,	BE, BG, CH, CY, CZ,	DE, DK, EE, ES,			
FI, FR, GB	, GR, HU, IE, IT,	LU, MC, NL, PT, RO,	SE, SI, SK, TR,			
BF, BJ, CF	, CG, CI, CM, GA,	GN, GQ, GW, ML, MR,	NE, SN, TD, TG			
CA 2496867	AA 20040311	CA 2003-2496867	20030828			
AU 2003278744	A1 20040319	AU 2003-278744	20030828			
EP 1539183	A1 20050615	EP 2003-770268	20030828			
R: AT, BE, CH	, DE, DK, ES, FR,	GB, GR, IT, LI, LU,	NL, SE, MC, PT,			
IE, SI, LT	, LV, FI, RO, MK,	CY, AL, TR, BG, CZ,	EE, HU, SK			
JP 2006506445	T2 20060223	JP 2004-569763	20030828			
PRIORITY APPLN. INFO.:		US 2002-407146P	P 20020828			
		US 2002-408332P	P 20020904			
		US 2003-479257P	P 20030617			
		WO 2003-US27186	W 20030828			
OTHER SOURCE(S):	MARPAT 140:2299	14				

The invention relates to the use of compds. to ameliorate or treat conditions such as a cystic fibrosis, neutropenia or other exemplified conditions. Exemplary compds. that can be used include  $3\beta$ -hydroxy- $17\beta$ -aminoandrost-5-ene,  $3\beta$ -hydroxy- $16\alpha$ -

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fluoro-17β-aminoandrost-5-ene, 3α-hydroxy-16α-fluoro-
     17β-aminoandrost-5-ene, 3β-hydroxy-16β-fluoro-17β-
     aminoandrost-5-ene, 1\alpha, 3\beta-dihydroxy-4\alpha-fluoroandrost-5-
     ene-17-one, lα,3β, 17β-trihydroxy-4α-fluorandrost-5-
     ene, 1\beta, 3\beta-dihydroxy-6\alpha-bromoandrost-5-ene,
     1\alpha-fluoro-3\beta, 12\alpha-dihydroxyandrost-5-ene-17-one,
     1\alpha-fluoro-3\beta, 4\alpha-dihydroxyandrost-5-ene and
     4\alpha-fluoro-3\beta, 6\alpha, 17\beta-trihydroxyandrostante.
REFERENCE COUNT:
                           2
                                 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
                                 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L13 ANSWER 15 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:
                           2004:198294 CAPLUS
DOCUMENT NUMBER:
                           140:241046
                           Stable oxazaphosphorine-2-mercaptoethanesulfonate
TITLE:
                           formulations
INVENTOR(S):
                           Daftary, Gautam Vinod; Pai, Srikanth Annappa;
                           Rivankar, Sangeeta Hanurmesh; Praveen, Kumar Subbappa
PATENT ASSIGNEE(S):
                           Bharat Serums & Vaccines Ltd., India
SOURCE:
                           Eur. Pat. Appl., 16 pp.
                           CODEN: EPXXDW
DOCUMENT TYPE:
                           Patent
LANGUAGE:
                           English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                           KIND
                                  DATE
                                               APPLICATION NO.
                                                                         DATE
     EP 1396268
                            Al
                                  20040310
                                               EP 2003-255566
                                                                         20030905
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     CA 2497898
                            AΑ
                                   20040318
                                                CA 2003-2497898
                                                                         20030904
     WO 2004022699
                            A2
                                   20040318
                                                WO 2003-IN298
                                                                         20030904
     WO 2004022699
                                   20050324
                            А3
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
              GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG,
              PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR,
         TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
              KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
              BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     BR 2003014068
                                   20050705
                                                BR 2003-14068
                                                                         20030904
                            А
     US 2005272698
                                                US 2005-529273
                                   20051208
                                                                         20050325
                            A1
                                                IN 2002-MU809
                                                                         20020905
PRIORITY APPLN. INFO.:
                                                                      А
                                                WO 2003-IN298
                                                                      W
                                                                         20030904
OTHER SOURCE(S):
                           MARPAT 140:241046
     Low toxicity, stable oxazaphosphorine-containing compns. are prepared by adding
     an oxazaphosphorine antineoplastic and a 2-mercaptoethanesulfonate to an
     aqueous solution of an etherified \beta- cyclodextrin. The
     2-mercaptoethanesulfonate can be added as an aqueous solution optionally containing
     an etherified \beta- cyclodextrin. Preferably, the
     oxazaphosphorine antineoplastic is iffosfamide, the 2-
     mercaptoethanesulfonate is Mesna and the etherified \beta-
     cyclodextrin is 2-hydroxypropyl-β-
     cyclodextrin. Thus, a formulation contained ifosfamide
     10, Mesna 2, 2-hydroxypropyl-β- cyclodextrin 40,
     disodium hydrogen phosphate 0.1, and sodium dihydrogen phosphate 0.06 g,
     and water qs to 200 mL.
                                  THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
REFERENCE COUNT:
                           5
                                  RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L13 ANSWER 16 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:
                           2003:22715 CAPLUS
DOCUMENT NUMBER:
                           138:61373
TITLE:
                           Modified-release oral pharmaceutical compositions
INVENTOR(S):
                           Massironi, Maria Gabriella
PATENT ASSIGNEE(S):
                           Farmatron Ltd., UK
                           PCT Int. Appl., 21 pp.
SOURCE:
                           CODEN: PIXXD2
DOCUMENT TYPE:
                           Patent
LANGUAGE:
                           English
FAMILY ACC. NUM. COUNT:
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PATENT INFORMATION:

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PATENT NO.
                          KIND DATE
                                              APPLICATION NO.
                                                                       DATE
                           A1
                                  20030109
                                              WO 2002-EP6749
                                                                       20020619
     WO 2003002151
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
         UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                           AA 20030109
                                            CA 2002-2451379
                                                                      20020619
     CA 2451379
                                  20040331
                                               EP 2002-747410
                                                                        20020619
     EP 1401501
                           A1
     EP 1401501
                           В1
                                  20050824
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
                                               JP 2003-508389
                                  20041118
                                                                        20020619
     JP 2004534833
                           Т2
     AT 302616
                                  20050915
                                               AT 2002-747410
                                                                        20020619
                           E.
                                               PT 2002-747410
     PT 1401501
                           T
                                  20051031
                                                                        20020619
                                               US 2004-482461
                                                                        20040617
     IIS 2004213844
                           A1
                                  20041028
                                               IT 2001-MI1337
                                                                    A 20010626
PRIORITY APPLN. INFO.:
                                               WO 2002-EP6749
                                                                    W 20020619
     The present invention relates to modified-release oral pharmaceutical
     compns. containing 1 or more active drugs solubilized, suspended or embedded
     in a suitably formulated amphiphilic matrix which, loaded in hydrophilic
     matrixes, provides different release profiles. Gelucire 44/14 (45 g) is
     melted and kept at 55-65^{\circ}, 5 g Transcutol is added and the stirred
     mixture is mixed with 5 g dioctyl sodium sulfosuccinate and 10 g \beta-
     cyclodextrin. Calcium folinate (75 g) is loaded into a
     granulator/homogenizer and the hot mixture obtained above is added thereto.
     The mixture is granulated to homogeneity, then 100 g hydroxypropyl
     Me cellulose and 50 mg Polycarbophil are added in the granulator. The
     components are mixed to a homogeneous dispersion of the matrixes, then 210
     g of Prosolv, 5 g magnesium stearate and 5 g colloidal silica are added in
     succession. The final mixture is tabletted to a unitary weight of 510
     mg/tablet, so that 75 mg active ingredient/single tablet are administered.
REFERENCE COUNT:
                          2
                                 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
                                 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L13 ANSWER 17 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:
                          2002:716321 CAPLUS
                          137:246527
DOCUMENT NUMBER:
                          Multivalent MHC constructs: Immunoanalysis, diagnosis
TITLE:
                          and therapy
INVENTOR(S):
                          Winther, Lars; Petersen, Lars Oestergaard; Buus,
                           Soeren; Schoeller, Joergen; Ruub, Erik; Aamellem,
                          Oevstein
PATENT ASSIGNEE(S):
                           Dako A/S, Den.; Dynal Biotech Asa
                           PCT Int. Appl., 304 pp.
SOURCE:
                           CODEN: PIXXD2
DOCUMENT TYPE:
                           Patent
LANGUAGE:
                          English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
                                                                        DATE
     PATENT NO.
                       - KIND
                                DATE
                                               APPLICATION NO.
                           ----
                                               ______
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     WO 2002072631
                           A2
                                  20020919
                                               WO 2002-DK169
                                                                        20020313
     WO 2002072631
                                  20021128
                           C1
     WO 2002072631
                           A3
                                  20031106
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
              LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
              PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
              KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
              GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
              GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2440773
                           AA
                                  20020919
                                               CA 2002-2440773
                                                                        20020313
                                               EP 2002-706685
     EP 1377609
                           A2
                                  20040107
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
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JP 2005500257
                                                                                     20050106
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                                                                    Т2
                                                                                                                    NO 2003-4020
                                                                                                                                                                                  20030911
            NO 2003004020
                                                                    Α
                                                                                     20031106
                                                                                                                                                                          A 20010314
PRIORITY APPLN. INFO.:
                                                                                                                    DK 2001-435
                                                                                                                    DK 2001-436
                                                                                                                                                                         A 20010314
                                                                                                                    DK 2001-441
                                                                                                                                                                          A 20010314
                                                                                                                    US 2001-275447P
                                                                                                                                                                         P 20010314
                                                                                                                    US 2001-275448P
                                                                                                                                                                          P 20010314
                                                                                                                    US 2001-275470P
                                                                                                                                                                         P 20010314
                                                                                                                    WO 2002-DK169
                                                                                                                                                                         W 20020313
            The authors disclose MHC mol. constructs (classical and non-classical)
            conjugated to soluble or insol. carriers wherein the affinity and avidity of
            the constructs exceed that of comparable MHC tetramers. In one example,
             the construct is comprised of biotinylated HLA-A2 bound to FITC-labeled
            streptavidin conjugated to soluble derivatized dextran. The above construct
            loaded with MART-1 or influenza virus peptides was shown to effect T-cell
             activation at a lower concentration than. Also comprised by the
            present invention is the sample-mounted use of MHC mols., MHC mol.
            multimers, and MHC mol. constructs.
L13 ANSWER 18 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
                                                                  2002:521462 CAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                                                                  137:88442
                                                                  Incensole and furanogermacrens and compounds in
TITLE:
                                                                   treatment for inhibiting neoplastic lesions and
                                                                  microorganisms
                                                                   Shanahan-Pendergast, Elisabeth
INVENTOR(S):
PATENT ASSIGNEE(S):
                                                                  Ire.
                                                                   PCT Int. Appl., 68 pp.
SOURCE:
                                                                  CODEN: PIXXD2
DOCUMENT TYPE:
                                                                  Patent
LANGUAGE:
                                                                  English
FAMILY ACC. NUM. COUNT:
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PATENT INFORMATION:
             PATENT NO.
                                                                  KIND
                                                                                  DATE
                                                                                                                    APPLICATION NO.
                                                                                                                                                                                   DATE.
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             WO 2002053138
                                                                   A2
                                                                                     20020711
                                                                                                                    WO 2002-IE1
                                                                                                                                                                                   20020102
                                                                                   20020919
            WO 2002053138
                                                                   A3

    W: AE, AG, AT, AU, BB, BG, CA, CH, CN, CO, CU, CZ, LU, LV, MA, MD, UA, UG, US, VN, YU, RU, TJ, TM
    RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, AT, BE, CH, CY, DE, ES, FI,

                                 ML, MR, NE, SN, TD, TG
             EP 1351678
                                                                    A2
                                                                                    20031015
                                                                                                                    EP 2002-727007
                                                                                                                                                                                   20020102
                        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
             US 2004092583
                                                                                                                                                                                20010102
PRIORITY APPLN. INFO.:
                                                                                                                     IE 2001-2
                                                                                                                     WO 2002-IE1
                                                                                                                                                                           W 20020102
                                                                  MARPAT 137:88442
OTHER SOURCE(S):
             The invention discloses the use of incensole and/or furanogermacrens,
             derivs. metabolites and precursors thereof in the treatment of neoplasia,
             particularly resistant neoplasia and immunodysregulatory disorders. These
             compds. can be administered alone or in combination with conventional
             chemotherapeutic, antiviral, antiparasite agents, radiation and/or % \left( 1\right) =\left( 1\right) \left( 1\right) 
              surgery. Incensole and furanogermacren and their mixture showed antitumor
              activity against various human carcinomas and melanomas and antimicrobial
              activity against Staphylococcus aureus and Enterococcus faecalis.
L13 ANSWER 19 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:
                                                                   2001:545502 CAPLUS
DOCUMENT NUMBER:
                                                                   135:117219
                                                                   Hapten-coagulation agent-antineoplastic agent
TITLE:
                                                                   combinations for treating neoplasms
INVENTOR(S):
                                                                   Yu, Baofa
 PATENT ASSIGNEE(S):
                                                                   USA
 SOURCE:
                                                                   PCT Int. Appl., 83 pp.
                                                                   CODEN: PIXXD2
DOCUMENT TYPE:
                                                                   Patent
 LANGUAGE:
                                                                   English
 FAMILY ACC. NUM. COUNT:
 PATENT INFORMATION:
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001052868	A1	20010726	WO 2001-US1737	20010118
WO 2001052868	C2	20030116		

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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
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             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
             ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                           AΑ
                                 20010726
                                              CA 2001-2397598
                                                                      20010118
     CA 2397598
     JP 2004505009
                           T2
                                 20040219
                                              JP 2001-552915
                                                                      20010118
PRIORITY APPLN. INFO.:
                                              US 2000-177024P
                                                                   P 20000119
                                                                   W 20010118
                                              WO 2001-US1737
    Methods are provided for treating neoplasms, tumors and cancers, using one
     or more haptens and coagulation agents or treatments, alone or in
     combination with other anti-neoplastic agents or treatments. Also
     provided are combinations, and kits containing the combinations for effecting
     the therapy.
                                THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS
REFERENCE COUNT:
                          8
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L13 ANSWER 20 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
                          1998:293427 CAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                          129:8597
TITLE:
                          Embedding and encapsulation of controlled release
                          particles
INVENTOR(S):
                          Van Lengerich, Bernhard H.
PATENT ASSIGNEE(S):
                          Van Lengerich, Bernhard H., USA
                          PCT Int. Appl., 63 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:
                          Patent
LANGUAGE:
                          English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                          KIND
                                 DATE
                                              APPLICATION NO.
                                                                      DATE
     WO 9818610
                          A1
                                 19980507
                                              WO 1997-US18984
                                                                      19971027
         W: AU, CA, JP, NO, PL, US
         RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
                           AA
                                 19980507
                                              CA 1997-2269806
     CA 2269806
                                                                      19971027
     CA 2269806
                                 20060124
                           С
     AU 9749915
                           A1
                                 19980522
                                              AU 1997-49915
                                                                      19971027
     AU 744156
                           B2
                                 20020214
     EP 935523
                           A1
                                 19990818
                                              EP 1997-912825
                                                                      19971027
     EP 935523
                           B1
                                 20040929
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
         R:
             IE, FI
     JP 2002511777
                                              JP 1998-520558
                           Т2
                                 20020416
     EP 1342548
                                 20030910
                                              EP 2003-10031
                                                                      19971027
                           A1
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     AT 277739
                           E
                                 20041015
                                              AT 1997-912825
                                                                      19971027
     NO 9902036
                                              NO 1999-2036
                                                                      19990428
                                 19990428
                           Α
PRIORITY APPLN. INFO.:
                                              US 1996-29038P
                                                                   P 19961028
                                              US 1997-52717P
                                                                   P 19970716
                                              EP 1997-912825
                                                                   A3 19971027
                                              WO 1997-US18984
                                                                   W 19971027
AB
     Controlled release, discrete, solid particles which contain an
     encapsulated and/or embedded component such as a heat sensitive or readily
     oxidizable pharmaceutically, biol., or nutritionally active component are
     continuously produced without substantial destruction of the matrix
     material or encapsulant. A release-rate controlling component is
     incorporated into the matrix to control the rate of release of the
     encapsulant from the particles. The addnl. component may be a hydrophobic
     component or a high water binding capacity component for extending the
     release time. The plasticizable matrix material, such as starch, is
     admixed with at least one plasticizer, such as water, and at least one
     release-rate controlling component under low shear mixing conditions to
     plasticize the plasticizable material without substantially destroying the
     at least one plasticizable material and to obtain a substantially
     homogeneous plasticized mass. The plasticizer content is substantially
     reduced and the temperature of the plasticized mass is substantially
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reduced prior to admixing the plasticized mass with the

encapsulant to avoid substantial destruction of the encapsulant and to obtain a formable, extrudable mixture The mixture is extruded though a die

without substantial or essentially no expansion and cut into discrete, relatively dense particles. Release properties may also be controlled by precoating the encapsulant and/or coating the extruded particles with a film-forming component. An example of encapsulation of acetylcysteine is given using starch, polyethylene, glycerol monostearate, and vegetable oil.

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 21 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

1997:684284 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 127:322811

TITLE: 5-androstene-3 $\beta$ ,17 $\alpha$ -diol as an inhibitor of

tumor growth Loria, Roger M., USA INVENTOR(S): PATENT ASSIGNEE(S): SOURCE: PCT Int. Appl., 19 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PATENT NO.						APPLICATION NO.					DATE						
	9737						1997	1016	WO	19	97-l	JS58	49		1	9970	410	
	RW:	ΑT,	BE,	CH,	DE,	DK,	ES,	FI,	FR, GI	В,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE
CA	2252	110			AΑ		1997	1016	CA	19	97-2	2252	110		1	9970	410	
EP	9250	64			A1		1999	0630	EP	19	97-9	9202	44		1	9970	410	
EP	9250	64			B1		2003	0625										
	R:		BE, FI	•	DE,	DK,	ES,	FR,	GB, GI	R,	IT,	LI,	LU,	NL,	SE,	MC,	PT,	
JP	2000	5086	43		Т2		2000	0711	JP	19	97-	5364	54		1	9970	410	
AT	2435	18			E		2003	0715	AT	19	97-	9202	44		1	9970	410	
EP	1362	591			A1		2003	1119	EP	20	03-	1419	3		1	9970	410	
EP	1362	591			В1		2005	1207										
	R:	•	BE, SI,			DK,	ES,	FR,	GB, G	R,	IT,	LI,	LU,	NL,	SE,	MC,	PT,	
PT	9250	64	•	•	Т		2003	1128	PT	19	97-	9202	44		1	9970	410	
ES	2202	606			Т3				ES									
AT	3118	86			E		2005	1215	AT	20	03-	1419	3		1	9970	410	
PRIORIT	Y APP	LN.	INFO.	. :									2 P					
									US	19	96-	1898	5P		P 1	9960	604	
									EΡ	19	97-	9202	44		A3 1	9970	410	
									WO	19	97-1	JS58	49	,	W 1	9970	410	
						~~~	107											

OTHER SOURCE(S): MARPAT 127:322811

The invention provides means of accelerating cell aging and programmed cell death in tumor cells by administration of  $3\beta$ ,  $17\alpha$ and rostenediol ( $\alpha AED$ ) or its ethers or esters. Pharmaceutical compns. containing 5-androstene-3 $\beta$ ,17 $\alpha$ -diol and a second anticancer drug also are claimed.

L13 ANSWER 22 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:183398 CAPLUS

DOCUMENT NUMBER: 118:183398

TITLE: Combination therapy using bioflavonoid or related

compounds with anti-cancer drugs

INVENTOR(S): Markaverich, Barry M.; Varma, Rajender Singh Baylor College of Medicine, USA

PATENT ASSIGNEE(S):

SOURCE: PCT Int. Appl., 35 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent English LANGUAGE:

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

OTHER SOURCE(S):

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9301824	Al	19930204	WO 1992-US6087	19920717
W: AU, CA, JP RW: AT, BE, CH,	DE, DK	, ES, FR, (	GB, GR, IT, LU, MC, N	NL, SE
AU 9223939	A1	19930223	AU 1992-23939	19920717
PRIORITY APPLN. INFO.:			US 1991-738044	A 19910724
			WO 1992-US6087	A 19920717

MARPAT 118:183398

Bioflavonoid compds. or related compds. are used in combination with AR antitumor agents for regulation of  $\operatorname{cell}$  growth and proliferation in normal and malignant tissues. The antitumor agents (antimetabolites, antibiotics, alkylating agents) may be combined with Me p-hydroxyphenylactate, its analogs, chemical derivs. and chemical related compds., phenylmethylene ketones, nitroalkenes, aurones, or chalcones for an enhanced inhibitor composition Thus, 100% (5/5) of mice bearing estrogen-dependent mammary tumors (T-511R) treated with a combination of 4,4'-hydroxychalcone (MV-88) and 5-fluorouricil had no signs of tumor on days 32 and 46; tumors returned in all animals following discontinuation of the treatment.

L13 ANSWER 23 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:614844 CAPLUS

DOCUMENT NUMBER: 115:214844

TITLE: Cyclodextrin inclusion complexes for drug

delivery compositions

INVENTOR(S):

Palmer, Clive Frederick Australian Commercial Research and Development Ltd., PATENT ASSIGNEE(S):

Australia

SOURCE: PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	CENT	NO.			KIND DATE				1	APPL	ICAT:		DATE				
WO	9104	026			A1		1991	0404	1	WO 1	990-2	AU41	8		1	9900	914
	W:	AT,	ΑU,	BB,	BG,	BR,	CA,	CH,	DE,	DK,	ES,	FI,	GB,	ΗU,	JP,	ΚP,	KR,
		LK,	LU,	MC,	MG,	MW,	NL,	NO,	RO,	SD,	SE,	SU,	US				
	RW:	ΑT,	BE,	BF,	ВJ,	CF,	CG,	CH,	CM,	DE,	DK,	ES,	FR,	GΑ,	GB,	IT,	LU,
		ML,	MR,	NL,	SE,	SN,	TD,	TG									
AU	9064	238			A1		1991	0418	ž	AU 1	990-		1	9900	914		
EP	4918	12			Al 19920701				EP 1990-914097						19900914		
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	IT,	LI,	LU,	NL,	SE			
PRIORITY	PRIORITY APPLN. INFO.:								i	AU 1	989-	6355			A 1	9890	914
									7	AU 1	989-	6356			A 1	9890	914
									1	AU 1	989-	6913			A 1	9891	017
									1	WO 1	990-2	AU41	8		A 1	9900	914

Inclusion complexes comprise (un)substituted cyclodextrin or salt thereof and pharmaceutical, pesticidal, herbicidal, agricultural, cosmetic or personal care agents or pharmacol. active derivs. or metabolites thereof. Methods for improving solubility of these agents in a neutral or acidic solution, improving the bioavailability of these agents, and decreasing the gastric irritation of naproxen, by forming inclusion complexes comprising the agents and (un)substituted cyclodextrins are also disclosed. Methods for treating mammals by orally or parenterally administering the foregoing pharmaceutical compns. are also provided. Amiodarone was triturated with di-Me  $\beta$ cyclodextrin,  $\alpha$ -cycloderxtrin, or  $\beta$ cyclodextrin in a 2:1 molar ratio and filled into hard gelatin capsules. The 3 inclusion complexes had improved oral amidarone absorption in pigs. There was a prolonged absorption of drug from the  $\,$ formulations without any marked compromise in the magnitude of peak drug concns.

L14 ANSWER 1 OF 31 MEDLINE ON STN
ACCESSION NUMBER: 2003057132 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12543700

TITLE: Efficacy of amphotericin B or itraconazole in a murine

model of central nervous system Aspergillus infection. Chiller Tom M; Sobel Raymond A; Luque Javier Capilla;

Clemons Karl V; Stevens David A

CORPORATE SOURCE: Division of Infectious Diseases, Department of Medicine, Santa Clara Valley Medical Center, San Jose, California

95128-2699, USA.

SOURCE: Antimicrobial agents and chemotherapy, (2003 Feb) 47 (2)

813-5.

Journal code: 0315061. ISSN: 0066-4804.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

AUTHOR:

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200308

ENTRY DATE: Entered STN: 20030206

Last Updated on STN: 20030809 Entered Medline: 20030808

AB Given the greater than 90% lethality of clinical central nervous system (CNS) aspergillosis despite current therapies, there is a need for an animal model to study therapeutic strategies. We previously established a model of CNS aspergillosis by intracerebral infection and report here the results of treatment with the two therapies with the greatest clinical experience, i.e., treatments with amphotericin B (AMB) and itraconazole (ITZ). Mice were given cyclophosphamide to produce pancytopenia. AMB was given intraperitoneally (i.p.; 3 mg/kg of body weight) or intravenously (i.v.; 0.8 mg/kg) once daily. ITZ in cyclodextrin was given by gavage once daily at a dose of 100 mg/kg or twice daily at 50 mg/kg. Treatments were started at day 1 postinfection and given for 10 days. At day 15, survivors were euthanatized. Ninety percent of the mice given no treatment died by day 6, and 100% died by day 10. Mice treated with AMB either i.p. or i.v. had 40% survival. Mice treated with ITZ either once or twice per day had a median survival time of 10 days, compared with 4 days for control animals, but a survival rate of only 10%. AMB and ITZ prolonged survival (P, <0.0001 to <0.05) compared with controls. Brains from surviving mice had CFU of Aspergillus fumigatus. This model can be used to compare newer antifungals and to study combination therapy or immunotherapy to find better therapeutic alternatives.

L14 ANSWER 2 OF 31 MEDLINE ON STN
ACCESSION NUMBER: 94165171 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8120109

TITLE: Determination of the enantiomers of **ifosfamide** 

and its 2- and 3-N-dechloroethylated metabolites in plasma and urine using enantioselective gas chromatography with

mass spectrometric detection.

AUTHOR: Granville C P; Gehrcke B; Konig W A; Wainer I W

CORPORATE SOURCE: Department of Oncology, McGill University, Montreal, Que.,

Canada.
SOURCE: Journal

Journal of chromatography, (1993 Dec 8) 622 (1) 21-31.

Journal code: 0427043. ISSN: 0021-9673.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199404

ENTRY DATE: Entered STN: 19940412

Last Updated on STN: 19970203 Entered Medline: 19940405

AF rapid, sensitive, enantioselective gas chromatographic method has been developed for the quantitation of the enantiomers of **ifosfamide**(IFF) and its 2- and 3-dechloroethylated metabolites (2-DCE-IFF and 3-DCE-IFF) in human and animal plasma and human urine. IFF and the two dechloroethylated metabolites were extracted into chloroform, enantioselectively resolved by gas chromatography on a chiral stationary phase based upon heptakis(2,6-di-O-methyl- 3-O-pentyl)-beta
cyclodextrin and quantitated using mass-selective detection with selected-ion monitoring. The limits of quantitation for the enantiomers of IFF, 2-DCE-IFF and 3-DCE-IFF in plasma were 250 and 500 ng/ml respectively. In urine, the limits of quantitation for the enantiomers of IFF, 2-DCE-IFF and 3-DCE-IFF were 500 ng/ml. The method can detect

concentrations as low as 250 ng/ml of each enantiomer of 2- and 3-DCE-IFF in plasma and urine. The intra- and inter-day coefficients of variation for this method were with one exception less than 8%. The assay was validated for enantioselective pharmacokinetic studies in humans and rats and is the first reported enantioselective assay for the measurement of the enantiomers of 2- and 3-DCE-IFF in plasma.

L14 ANSWER 3 OF 31 MEDLINE on STN ACCESSION NUMBER: 90146247 MEDITUE.

DOCUMENT NUMBER: PubMed ID: 2619273 TITLE:

Oral and parenteral therapy with saperconazole (R 66905) of

invasive aspergillosis in normal and immunocompromised

animals.

Van Cutsem J; Van Gerven F; Janssen P A AUTHOR: CORPORATE SOURCE:

Janssen Research Foundation, Beerse, Belgium.

Antimicrobial agents and chemotherapy, (1989 Dec) 33 (12) SOURCE:

Journal code: 0315061. ISSN: 0066-4804.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199003

Entered STN: 19900328 ENTRY DATE:

Last Updated on STN: 19900328 Entered Medline: 19900306

Saperconazole (R 66905) is a broad-spectrum antifungal triazole with potent in vitro activity against Aspergillus spp. A total of 279 strains were tested in brain heart infusion broth. Development of the Aspergillus spp. was completely inhibited at 0.1 and 1 microgram of saperconazole per ml for 80.3 and 99.6% of the strains, respectively. Normal and immunocompromised guinea pigs were infected intravenously with Aspergillus fumigatus and treated orally, intravenously, or intraperitoneally with saperconazole or intraperitoneally with amphotericin B. Leukopenia, neutropenia, lymphocytosis, and monocytosis were obtained with mechlorethamine hydrochloride; leukopenia, neutrophilia, and lymphopenia were obtained with cyclophosphamide. Saperconazole was dissolved for oral treatment in polyethylene glycol and for parenteral treatment in **cyclodextrins**. Amphotericin B was given parenterally as Fungizone (E.R. Squibb & Sons). Treatment was given once daily for 14 days. An early starting treatment was efficacious, but the activity of saperconazole was maintained even when the onset of the treatment was delayed to the moribund state. The activity of saperconazole was not altered in immunocompromised animals. Saperconazole was clearly superior to amphotericin B and free of side effects. The oral and parenteral formulations of saperconazole were equipotent. The systemic activity of saperconazole in guinea pigs was confirmed in invasive aspergillosis in pigeons.

L14 ANSWER 4 OF 31 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN ACCESSION NUMBER: 2002:509385 BIOSIS

ACCESSION NUMBER: DOCUMENT NUMBER: PREV200200509385

TITLE: The efficacy of amphotericin B and itraconazole alone and

in combination in a murine model of CNS Aspergillus infection.

AUTHOR(S): Chiller, T. M. [Reprint author]; Luque, J. Capilla;

Clemons, K. V. [Reprint author]; Sobel, R. A. [Reprint

author]; Stevens, D. A. [Reprint author]

CORPORATE SOURCE: Stanford, CA, USA

SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2001) Vol. 41, pp. 391. print.

Meeting Info.: 41st Annual Meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy. Chicago, Illinois, USA. September 22-25, 2001.

DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 2 Oct 2002

Last Updated on STN: 2 Oct 2002

Background: Given the >95% lethality of clinical CNS aspergillosis with current therapies, there is a need for an animal model to study therapeutic strategies. We established a CNS model by intracerebral infection with Aspergillus and examined treatment with amphotericin B (AmB) and itraconazole (ITZ) alone and in combination. Methods: Male 5-week CD-1 mice were given  ${\it cyclophosphamide}\ 200{\it mg/kg}\ d\ -2$  then q5 d to produce pancytopenia. Groups of 10 were infected intracerebrally with 5X106 A. fumigatus conidia. AmB was given intraperitoneally (ip) at 3 mg/kg or intravenously (iv) at 0.8 mg/kg once daily. ITZ in cyclodextrin was given by gavage once-daily at 100 mg/kg or twice daily at 50 mg/kg. Treatments were started d 1 postinfection and given for 10 d. At d 15 survivors were euthanized and organ fungal burdens determined. Results: 90% of mice given no treatment died by d 6, 100% by d 10. Mice treated with AmB either ip or iv had 40% survival d 15. Mice treated with ITZ either once or twice/d had LD50 d 11 compared with d 4for controls but only 10% survival at d 15. AMB and ITZ prolonged survival (P<.01) vs. controls but were equal. All brains from surviving mice had CFUs of Aspergillus. Similar results were seen in repeated experiments. The combination of AMB ip and ITZ had an 70% survival at d 15, but not better (P>0.05) vs. either alone. Conclusions: Amb and ITZ alone and in combination significantly improves survival of mice infected with cerebral aspergillosis. The combination showed a trend toward better survival. This model could be used to study newer antifungals and/or immunotherapies to find better alternatives to treat CNS aspergillosis.

L14 ANSWER 5 OF 31 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1992:403652 BIOSIS

DOCUMENT NUMBER: PREV199243059527; BR43:59527 14 SULFATE BETA CYCLODEXTRIN SCD-TITLE:

TETRAHYDROCORTISOL THC AND-OR MINOCYCLINE MINO AS

MODULATORS OF ANTITUMOR AGENTS.

ALVAREZ SOTOMAYOR E [Reprint author]; TEICHER B A; HOLDEN S AUTHOR(S):

DANA-FARBER CANCER INSTITUTE, BOSTON, MASS 02115, USA CORPORATE SOURCE: SOURCE:

Proceedings of the American Association for Cancer Research

Annual Meeting, (1992) Vol. 33, pp. 420. Meeting Info.: 83RD ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, SAN DIEGO, CALIFORNIA, USA, MAY 20-23, 1992. PROC AM ASSOC CANCER RES ANNU MEET.

ISSN: 0197-016X.

DOCUMENT TYPE: Conference; (Meeting)

FILE SEGMENT: BR

LANGUAGE: ENGLISH

Entered STN: 26 Aug 1992 ENTRY DATE:

Last Updated on STN: 1 Oct 1992

L14 ANSWER 6 OF 31 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights

reserved on STN

ACCESSION NUMBER: 2005397930 EMBASE

TITLE: Making sense of itraconazole pharmacokinetics.

AUTHOR: Prentice A.G.; Glasmacher A.

A.G. Prentice, Department of Haematology, Royal Free CORPORATE SOURCE: Hospital, Pond Street, London NW3 2QG, United Kingdom.

archie.prentice@royalfree.nhs.uk

SOURCE: Journal of Antimicrobial Chemotherapy, (2005) Vol. 56, No.

SUPPL. 1, pp. i17-i22. .

Refs: 39 ISSN: 0305-7453 CODEN: JACHDX

COUNTRY: United Kingdom DOCUMENT TYPE: Journal; Article FILE SEGMENT: 004 Microbiology 030 Pharmacology

037 Drug Literature Index 038 Adverse Reactions Titles

039 Pharmacv

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20050922

Last Updated on STN: 20050922

AB The triazole, itraconazole, has a wide spectrum of antifungal activity in vitro. Confirming this activity in vivo has been a long and difficult task because of problems with formulation, delivery and uncertainty about effective bioavailability. The physicochemical properties of the drug make it insoluble in water but strongly protein bound. The absorption and blood levels of the original capsular formulation were predictable with non-linear, saturation kinetics in normal volunteers. Tissue penetration was high and sustained. In neutropenic patients with haematological malignancies, levels were very variable and the doses required to achieve effective antifungal levels were higher than predicted from normal subjects' results. The solubility of the drug and predictability of blood levels were improved by the formulation of an oral solution with cyclodextrin. Wash-out times were prolonged in patients with this new formulation implying that tissue penetration was maintained. A high

volume of distribution suggests that loading may be necessary. An intravenous cyclodextrin solution is also now available allowing rapid loading and avoidance of the well-known gut side effects of the oral solution. Clinical studies have suggested minimum bioavailable dosage and minimum trough blood levels for effective prophylaxis against systemic fungal infection. Interactions are also now well documented and manageable. The drug can be measured reliably, quickly and comparatively cheaply by HPLC in serum and plasma. The frequency of such testing in clinical practice depends on the need to ensure adequate levels and to avoid unwanted toxicity. .COPYRGT. The Author 2005. Published by Oxford University Press on behalf of the British Society for Antimicrobial Chemotherapy. All rights reserved.

L14 ANSWER 7 OF 31 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2002203515 EMBASE

TITLE: [Crystalline modifications and polymorphism changes during

drug manufacture).

MODIFICATIONS CRISTALLINES ET TRANSFORMATIONS POLYMORPHES

AU COURS DES OPERATIONS GALENIQUES.

AUTHOR: Doelker E.

CORPORATE SOURCE:

E. Doelker, Lab. de Pharmacie Galenique, Section de pharmacie, Universite de Geneve, Quai Ernest-Ansermet 30,

CH-1211 Geneve 4, Switzerland

SOURCE: Annales Pharmaceutiques Francaises, (2002) Vol. 60, No. 3,

pp. 161-176. .

Refs: 96

ISSN: 0003-4509 CODEN: APFRAD

COUNTRY: France

DOCUMENT TYPE: Journal; General Review Pharmacology FILE SEGMENT: 030

037 Drug Literature Index

039 Pharmacy

LANGUAGE: French

SUMMARY LANGUAGE: English; French

ENTRY DATE: Entered STN: 20020627

Last Updated on STN: 20020627

More than half of the pharmaceutical compounds exhibit polymorphism or pseudopolymorphism, e.g., they exist as more than one crystalline structure (true polymorphs, hydrates, solvates) or as more or less amorphous products. As such, they show at the solid state different physicochemical properties (melting point, transition point, plasticity, solubility, hygroscopicity, chemical reactivity), which in turn may affect the technological and biopharmaceutical properties of active ingredients or excipients (compactibility, dissolution rate, bioavailability, pharmacological activity, stability). When considering a chemically well-defined compound, one may find one or another crystalline state or polymorphic form according to the source or batch considered. One may also observe changes in technological or biopharmaceutical properties that are due to polymorphic transformations arising from the mechanical or heat treatment or from the environmental conditions (solvent-mediated reactions, desolvation) undergone by the product or the dosage form. present article presents the fundamental aspects related to the above-mentioned phenomena and reviews both classical and recent examples from the literature reporting transformations during milling or grinding, tabletting, preparation of drug suspensions, granulation, dissolution or release tests, stability trials, spray drying, freeze-drying or preparation of adsorbates or complexes.

L14 ANSWER 8 OF 31 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2002126074 EMBASE

TITLE: Companion animal parasitology: A clinical perspective.

AUTHOR: Irwin P.J.

CORPORATE SOURCE: P.J. Irwin, Sch. of Veterinary Clinical Science, Div. of

Veterinary/Biomed. Science, Murdoch University, Murdoch, WA

6150, Australia. irwinp@numbat.murdoch.edu.au

SOURCE: International Journal for Parasitology, (2002) Vol. 32, No.

5, pp. 581-593. .

Refs: 97

ISSN: 0020-7519 CODEN: IJPYBT

PUBLISHER IDENT .: S 0020-7519(01)00361-7

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Conference Article FILE SEGMENT: Drug Literature Index 037

LANGUAGE: English SUMMARY LANGUAGE: English

Entered STN: 20020418 ENTRY DATE:

Last Updated on STN: 20020418

In recent years there have been many changes to the ways that clinical veterinary science is conducted and nowhere is this more evident than in companion animal practice. Veterinarians working with pet dogs and cats are facing new challenges associated with the emergence and re-emergence of parasitic diseases. Some, such as Neospora caninum, have been recently recognised; others like Giardia and Cryptosporidium have been reported with increasing frequency, in part as a result of laboratory tests with improved sensitivity and specificity. In many regions, the emergence of parasitic diseases has been a consequence of pet travel and exotic diseases pose a unique diagnostic challenge for the veterinarian, as the index of suspicion for these conditions may be absent. The ranges of certain vector-borne diseases such as babesiosis, hepatozoonosis, ehrlichiosis, leishmaniasis and dirofilariasis are extending due to ecological and climatic changes and enhanced by animals with subclinical infection returning home from endemic areas. In companion animal practice, veterinarians have the additional responsibility of providing accurate information about the zoonotic transmission of parasite infections from pets, especially to those most vulnerable such as children, the elderly and the immunocompromised. Effective education is vital to allay public concerns and promote responsible pet ownership. .COPYRGT. 2002 Australian Society for Parasitology Inc. Published by Elsevier Science Ltd. All rights reserved.

L14 ANSWER 9 OF 31 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER:

2001407641 EMBASE

TITLE:

Infectious complications within the first year after

nonmyeloablative allogeneic peripheral blood stem cell

transplantation.

AUTHOR:

Mossad S.B.; Avery R.K.; Longworth D.L.; Kuczkowski E.M.;

McBee M.; Pohlman B.L.; Sobecks R.M.; Kalaycio M.E.; Andresen S.W.; Macklis R.M.; Bolwell B.J.

CORPORATE SOURCE:

Dr. S.B. Mossad, Department of Infectious Diseases,

Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland,

OH 44195, United States

SOURCE:

Bone Marrow Transplantation, (2001) Vol. 28, No. 5, pp.

491-495.

Refs: 19

ISSN: 0268-3369 CODEN: BMTRE

COUNTRY: DOCUMENT TYPE: United Kingdom Journal; Article

FILE SEGMENT:

006 Internal Medicine

Hematology 025

037 Drug Literature Index

LANGUAGE: English SUMMARY LANGUAGE: English

ENTRY DATE:

Entered STN: 20011206

Last Updated on STN: 20011206

Nonmyeloablative peripheral blood stem cell transplantation (PBSCT) is a novel therapeutic strategy for patients with malignant and non-malignant hematologic diseases. Infectious complications of this procedure have not been previously well described. Data on 12 patients transplanted at a tertiary care center were collected prospectively and verified retrospectively. Neutropenia developed in a third of patients, lasting for a median of 5 days. All patients developed some degree of graft-versus-host disease, as intended. Most patients achieved full chimerism by week 5. Bacterial infections occurred in two patients (17%). Cytomegalovirus (CMV) viremia occurred in five patients (42%) at a median of 80 days; none had received CMV prophylaxis. Viremia was associated with fever and fatigue in three patients, possible gastrointestinal involvement in one patient and was asymptomatic in one patient. All viremic patients responded to intravenous ganciclovir therapy. No fungal infections were documented. No patients died as a result of infection. The incidence of CMV viremia in our patients was high, but the incidence of invasive disease due to CMV was low. The best strategy to prevent CMV in patients undergoing nonmyeloablative PBSCT remains to be determined, but strategies employed in traditional allogeneic bone marrow transplantation should be considered in these patients.

L14 ANSWER 10 OF 31 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1998315940 EMBASE

TITLE:

Pharmaceutical aspects of paclitaxel.

AUTHOR:

Panchagnula R.

CORPORATE SOURCE:

R. Panchagnula, Department of Pharmaceutics, NIPER,

SOURCE:

Nagar-160062 (Punjab), India. niper@chd.nic.in International Journal of Pharmaceutics, (1998) Vol. 172,

No. 1-2, pp. 1-15. .

Refs: 114

ISSN: 0378-5173 CODEN: IJPHDE

PUBLISHER IDENT .: COUNTRY:

S 0378-5173(98)00188-4 Netherlands

DOCUMENT TYPE:

Journal; General Review

FILE SEGMENT:

030 Pharmacology

037 Drug Literature Index

038 Adverse Reactions Titles

039 Pharmacy

LANGUAGE: SUMMARY LANGUAGE:

Enalish English

Entered STN: 19981015

ENTRY DATE:

Last Updated on STN: 19981015

Paclitaxel is one of the most important lead compounds to emerge from a natural source. Because of the complex and unusual chemistry of paclitaxel, it is mainly extracted from the bark of a slow growing Western yew. Although total chemical synthesis of paclitaxel has been achieved, it may not be feasible commercially. Paclitaxel has a low therapeutic index: it is highly lipophilic and practically insoluble in water. The commercially available injection preparation is a sterile solution of the drug in Cremophor® EL and dehydrated alcohol. Present-day cancer chemotherapy with paclitaxel frequently causes hypersensitivity reactions. The major hurdles for successful therapy with paclitaxel are the availability of the drug and its delivery. The importance of developing an improved delivery system for paclitaxel is obvious from the problems seen from present-day therapy. Hence, the current approaches are mainly focused on: (1) developing formulations that are devoid of Cremophor® EL, (2) the possibility of large-scale preparation; and (3) stability for longer periods of time. The path to identify new molecules with better therapeutic efficacy will continue to be an integral part of health care systems, but the author is emphasizing the importance of 'better delivery of drugs' which is going to further refine the therapy. The different approaches investigated so far have shown much promise in replacing the Cremophor® based vehicle for paclitaxel delivery. However, the final product for human use is still far away. Therefore this review is the first comprehensive account of the pharmaceutical aspects of paclitaxel, with special emphasis on its delivery. Copyright (C) 1998 Elsevier Science B.V.

L14 ANSWER 11 OF 31 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER:

1998213146 EMBASE

TITLE:

[Direct gaschromatographic separation of drug racemates]. ZUR DIREKTEN GASCHROMATOGRAPHISCHEN ENANTIOMERENTRENNUNG

VON ARZNEISTOFFRACEMATEN.

AUTHOR: CORPORATE SOURCE: Schleuder M.; Durrbeck A.; Jira T. Dr. M. Schleuder, Institut fur Pharmazie,

Ernst-Moritz-Arndt-Univ. Greifswald, Friedrich-Ludwig-Jahn-

Str. 17, D-17489 Greifswald, Germany Pharmazie, (1998) Vol. 53, No. 6, pp. 381-386. .

SOURCE: Refs: 22

ISSN: 0031-7144 CODEN: PHARAT

COUNTRY:

Germany

DOCUMENT TYPE: FILE SEGMENT:

Journal; Article

030 Pharmacology 037

Drug Literature Index

039 Pharmacy German

LANGUAGE:

SUMMARY LANGUAGE:

English; German

ENTRY DATE:

Entered STN: 19980806

Last Updated on STN: 19980806

For inspection of the direct separability of synthetic drug racemates through GC/MS a uniform scheme is proposed and checked with 35 drugs and two cyclodextrin capillary columns. All investigated analytes vaporized without decomposition, 26 of them are separable in the enantiomers, among them 10 with separation to the baseline and 14 with CO-NH-structure.

L14 ANSWER 12 OF 31 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1998153576 EMBASE

Oral dosage forms that should not be crushed: 1998 update. TITLE:

AUTHOR: Mitchell J.F.

CORPORATE SOURCE: J.F. Mitchell, Medical Education Systems, 5840 North Canton

Center Road, Canton, MI 48187, United States Hospital Pharmacy, (1998) Vol. 33, No. 4, pp. 399-415. . SOURCE:

Refs: 2

ISSN: 0018-5787 CODEN: HOPHAZ

United States COUNTRY:

DOCUMENT TYPE: Journal; (Short Survey)

FILE SEGMENT: Drug Literature Index 037

039 Pharmacv

LANGUAGE: English English SUMMARY LANGUAGE:

ENTRY DATE: Entered STN: 19980702

Last Updated on STN: 19980702

The purpose of this feature, last published in this journal in 1996, is to alert health care practitioners about medications that should not be crushed because of their special pharmaceutical formulations. Alternative, liquid forms of these products are listed when they are

available. In addition to regular updates in Hospital Pharmacy, 'Oral Dosage Forms That Should Not Be Crushed' is reproduced yearly in the American Drug Index.

L14 ANSWER 13 OF 31 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights

reserved on STN

ACCESSION NUMBER: 96146586 EMBASE

DOCUMENT NUMBER: 1996146586

TITLE: Use of principal component analysis for the study of the

retention behaviour of anticancer drugs on  $\beta$ -

cyclodextrin polymer-coated silica column.

AUTHOR: Cserhati T.; Forgacs E.

CORPORATE SOURCE: Central Res. Institute for Chemistry, P.O. Box 17, H-1525

Budapest, Hungary

Journal of Chromatography A, (1996) Vol. 728, No. 1-2, pp. SOURCE:

67-73.

ISSN: 0021-9673 CODEN: JCRAEY

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 016 Cancer

037 Drug Literature Index

LANGUAGE: English SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 960604

Last Updated on STN: 960604

The retention parameters of eighteen commercial anticancer drugs were determined on a  $\beta$ - cyclodextrin polymer-coated silica support ( $\beta$ CDP) using methanol-water mixtures as eluent and the relationship between the retention behaviour and physico-chemical parameters was elucidated by principal component analysis (PCA) followed by two-dimensional non-linear mapping. No significant linear correlation was found between the retention behaviour of drugs on octadecylsilica and  $\beta$ CDP silica columns, indicating that the retention capacity and selectivity of the columns are considerably different. The results of PCA indicated that hydrophobic and electronic interactions and steric conditions govern the retention of anticancer drugs on  $\beta$ CDP column, suggesting a mixed retention mechanism.

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reserved on STN

ACCESSION NUMBER: 95262462 EMBASE

DOCUMENT NUMBER: 1995262462

TITLE: Interaction of some anticancer drugs with

carboxymethyl-β- cyclodextrin.

AUTHOR: Cserhati T.

Central Res. Institute for Chemistry, Hungarian Academy of CORPORATE SOURCE:

Sciences, P.O. Box 17,1525 Budapest, Hungary

SOURCE: International Journal of Pharmaceutics, (1995) Vol. 124,

No. 2, pp. 205-211. . ISSN: 0378-5173 CODEN: IJPHDE

COUNTRY: Netherlands DOCUMENT TYPE: Journal; Article FILE SEGMENT: Pharmacology 030

037 Drug Literature Index

LANGUAGE: English SUMMARY LANGUAGE: English

Entered STN: 950926 ENTRY DATE:

Last Updated on STN: 950926

The interaction between 23 anticancer drugs and carboxymethyl- $\beta$ -AB cyclodextrin (CM- $\beta$ -CD) was studied by reversed-phase charge-transfer thin-layer chromatography and the relative strength of interaction was calculated. CM-β-CD formed inclusion complexes with 13 compounds, the complex always being less hydrophobic than the uncomplexed drug. The inclusion-forming capacity of drugs differed considerably depending on their chemical structures. Principal component analysis indicated that the hydrophilic parameters (hydrophobicity, specific hydrophobic surface area) of drugs exert the greatest influence on the stability of CM- $\beta$ -CD-drug inclusion complexes.

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ACCESSION NUMBER:

95123776 EMBASE

DOCUMENT NUMBER:

1995123776

TITLE:

Interaction of taxol and other anticancer drugs with

a- cyclodextrin.

AUTHOR:

Cserhati T.; Forgacs E.; Hollo J.

CORPORATE SOURCE:

Central Research Institute for Chem., Hungarian Academy of Sciences, P.O. Box 17,1525 Budapest, Hungary

SOURCE:

Journal of Pharmaceutical and Biomedical Analysis, (1995)

Vol. 13, No. 4-5, pp. 533-541. ISSN: 0731-7085 CODEN: JPBADA

COUNTRY:

United Kingdom

DOCUMENT TYPE:

Journal; Conference Article

FILE SEGMENT:

Cancer

016

029 Clinical Biochemistry Drug Literature Index

037 LANGUAGE: English

SUMMARY LANGUAGE:

English

ENTRY DATE:

Entered STN: 950523

Last Updated on STN: 950523

The interaction between 23 anticancer drugs and  $\alpha\text{--}$  $\operatorname{\textbf{cyclodextrin}}$  ( $\alpha\text{-CD}$ ) was studied by reversed-phase charge-transfer thin-layer chromatography and the relative strength of interaction was calculated. As  $\alpha-CD$  has smaller cavity than  $\beta$ and  $\tau$ -CD it interacted only with 10 anticancer drugs proving the relatively poor complex forming capacity of  $\alpha$ -CD. The hydrophobicity of host-guest inclusion complex was always different from that of the uncomplexed drug suggesting that the complex formation may influence the uptake, absorption, half-life etc. of the original drug. The inclusion forming capacity of drugs differed considerably according to their chemical structure. The intensity of interaction significantly depended on the hydrophobicity of the guest molecule proving the preponderant role of hydrophobic interactions in inclusion complex formation.

L14 ANSWER 16 OF 31 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER:

95086887 EMBASE

DOCUMENT NUMBER:

1995086887

TITLE:

Charge-transfer chromatographic study of the complex

formation of some anticancer drugs with  $\gamma-$ 

cyclodextrin.

AUTHOR:

SOURCE:

COUNTRY:

CORPORATE SOURCE:

Central Research Inst. for Chemistry, Hungarian Academy of

Sciences, P.O. Box 17,1525 Budapest, Hungary Analytical Biochemistry, (1995) Vol. 225, No. 2, pp.

328-332.

ISSN: 0003-2697 CODEN: ANBCA2 United States

DOCUMENT TYPE: FILE SEGMENT:

Journal; Article Drug Literature Index

LANGUAGE: English English

SUMMARY LANGUAGE: ENTRY DATE:

Entered STN: 950420

Last Updated on STN: 950420

The interaction between 23 anticancer drugs and  $\gamma\text{--}$ cyclodextrin  $(\gamma$ -CD) was studied by reversed-phase charge-transfer thin-layer chromatography and the relative strength of interaction was calculated.  $\gamma$ -CD formed inclusion complexes with 14 compounds, the complex always being more or less hydrophobic than the uncomplexed drug. The inclusion-forming capacity of a drug differed considerably depending on its chemical structure. The linear correlation between the hydrophobicity and the specific hydrophobic surface area of

anticancer drugs indicated that they can be considered a homologous ries of compounds, although their chemical structures are highly different.

L14 ANSWER 17 OF 31 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights

reserved on STN

ACCESSION NUMBER: 87062869 EMBASE

DOCUMENT NUMBER: 1987062869

TITLE: Combined treatment for vesical cancer with pre- and

postoperative chemotherapy.

AUTHOR: Klimenko I.A.; Goikhberg M.I.; Zaparin V.K.; et al. CORPORATE SOURCE: Otdelenie Onkourologii s Gruppoj Radioizotopnykh

Issledovanij Kievskogo NI Instituta Urologii i Nefrologii,

Kiev, Ukraine

SOURCE: Urologiya i Nefrologiya, (1987) Vol. 52, No. 1, pp. 26-28.

CODEN: URNEAA

COUNTRY: Russia

DOCUMENT TYPE: Russia

Journal

FILE SEGMENT: 037 Drug Literature Index

LANGUAGE: Russian SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 911211

Last Updated on STN: 911211

L14 ANSWER 18 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:984057 CAPLUS

DOCUMENT NUMBER: 143:292623

TITLE: Biocompatible coating, method, and use of medical

surfaces

INVENTOR(S): Hoffmann, Erika

PATENT ASSIGNEE(S): Hemoteq G.m.b.H., Germany SOURCE: PCT Int. Appl., 38 pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: German FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005082434 WO 2005082434 WO 2005082434	A2 A3 B1	20050909 20051013 20051215	WO 2005-DE327	20050227
W: AE, AG, CN, CO, GE, GH, LK, LR, NO, NZ, SY, TJ, RW: BW, GH, AZ, BY, EE, ES, RO, SE,	AL, AM, AT, CR, CU, CZ, GM, HR, HU, LS, LT, LU, OM, PG, PH, TM, TN, TR, GM, KE, LS, KG, KZ, MD, FI, FR, GB,	, AU, AZ, BA, DE, DK, DM, ID, IL, IN, LV, MA, MD, PT, RO, TT, TZ, UA, RU, TJ, TM, GR, HU, IE	, BB, BG, BR, BW, , DZ, EC, EE, EG, , IS, JP, KE, KG, , MG, MK, MN, MW, , RU, SC, SD, SE, , UG, US, UZ, VC, , SD, SL, SZ, TZ, , AT, BE, BG, CH, , IS, IT, LT, LU, , CG, CI, CM, GA,	ES, FI, GB, GD, KP, KR, KZ, LC, MX, MZ, NA, NI, SG, SK, SL, SM, VN, YU, ZA, ZM, ZW UG, ZM, ZW, AM, CY, CZ, DE, DK, MC, NL, PL, PT,

PRIORITY APPLN. INFO.:

DE 2004-102004009850A 20040228 US 2004-551761P P 20040311

AB The invention relates to medical products having a surface that is at least partially covered by a polymer layer. Said polymer layer is preferably formed by autopolymm. Substances containing at least one multiple bond, especially unsatd. fatty acids comprising an alkyl chain consisting of preferably between 7 and 50 carbon atoms are polymerized. Other substances which do not participate in the polymerization can be added to the substances participating in the polymerization reaction. Said substances are preferably saturated fatty acids and fatty acid derivs. The invention also relates to methods for producing such medical products, and to the use of the same. Thus a non-expanding stent prepared from LVM 316 stainless steel was spray-coated with a mixture of linseed oil and paclitaxel at a ratio of 80:20 in chloroform at a ration of 1:1. Thereafter chloroform was evaporated and stored at 80°C.

L14 ANSWER 19 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:324038 CAPLUS

DOCUMENT NUMBER: 142:397825

TITLE:

Biocompatible, biostable coating of medical surfaces composed of polysulfone and hydrophilic polymers

INVENTOR(S):

Horres, Roland; Hoffmann, Michael; Faust, Volker;

Hoffmann, Erika; Di Biase, Donato

PATENT ASSIGNEE(S): Hemoteq G.m.b.H., Germany PCT Int. Appl., 57 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: German FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

1	PATENT NO.							KIND DATE				APPLICATION NO.						DATE			
7	NO.	2005	0326	11		A2	_	2005	0414	1	WO 2	2004-	DE21	84		2	0040	929			
		W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	вв,	BG,	BR,	BW,	BY,	ΒZ,	CA,	CH,			
			CN,	co,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,			
			GE,	GH,	GM,	HR,	ΗU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,			
			LK,	LR,	LS,	LT,	LU,	LV,	ΜA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,			
			NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	sc,	SD,	SE,	SG,	SK,	SL,	SY,			
	TJ, TM, TN				TN,	TR,	TT,	ΤZ,	UΑ,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW			
	RW: BW, GH, GM,		GM,	ΚE,	LS,	MW,	ΜZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,					
	AZ, BY, KG			KG,	ΚZ,	MD,	RU,	ТJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,				
			EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	NL,	PL,	PT,	RO,	SE,			
			SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,			
			SN,	TD,	TG																
1	DE	1020	0402	0856		A1		2005	0414		DE 2	2004-	1020	0402	0856	2	0040	428			
t	US 2005129731					A1		2005	0616	1	US 2	2004-	9799	77		2	0041	103			
PRIOR	PRIORITY APPLN. INFO.:										DE 2	2003-	1034	5132	7	A 2	0030	929			
											US 2	2003-	5162	95P	1	P 2	0031	103			
											DE 2	2004-	1020	0402	0856	A 2	0040	428			
										1	US 2	2004-	5715	82P	1	P 2	0040	517			
70 (	. The invention well														7						

AB The invention relates to medical products comprising at least one biocompatible biostable polysulfone coating. Said polysulfone coating makes it possible, via the admixt. of an adequate quantity of at least one hydrophilic polymer, to control the elution kinetics of the at least one antiproliferative, anti-inflammatory, antiphlogistic, and/or antithrombogenic agent that is introduced and/or applied while allowing different agents or agent concns. to be spatially separated with the aid of the layer system of biostable polymers. Also disclosed are a method for producing said medical products and the use thereof particularly in the form of stents for preventing restenosis. Thus a 2 g base-coat solution for spray coating contained 17.6 mg polyethersulfone(Udel form Solvay) in chloroform. The 3 g chloroformic topcoat solution included 25.2 g polyethersulfone and 1,2 mg PVP.

L14 ANSWER 20 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:453236 CAPLUS

DOCUMENT NUMBER:

141:17589

TITLE:

Activation of peptide prodrugs by human kallikrein 2

INVENTOR(S): Denmeade, Samuel R.; Isaacs, John T.; Lilja, Hans PATENT ASSIGNEE(S): The Johns Hopkins University, USA

SOURCE:

PCT Int. Appl., 48 pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA'	PATENT NO.						KIND DATE			APPLICATION NO.					DATE			
WO	2004	0461	69		A2		2004	0603	,	NO 2	003-	JS36	880		20	0031	118	
WO	2004	0461	69		C1		2005	0909										
	W:	ΑE,	AG,	AL,	AM,	AT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,	
		co,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	
		GM,	HR,	ΗU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,	
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NI,	NO,	ΝZ,	OM,	
	PG, PH, P				PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	ТJ,	TM,	TN,	
	TR, TT, T				UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW				
	RW:	BW,	GH,	GM,	ΚE,	LS,	MW,	MZ,	SD,	SL,	SZ,	ΤZ,	UG,	ZM,	ZW,	AM,	ΑZ,	
		BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	
		ES,	FI,	FR,	GB,	GR,	ΗU,	ΙE,	IT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	
		TR,	BF,	ΒJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG
CA	CA 2514089						2004	0603		CA 2	003-	2514	089		20	0031	118	
EP	1575		A2		2005	0921		EP 2	003-	7836	58		2	0031	118			
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙT,	LI,	LU,	NL,	SE,	MC,	PT,	
	IE, SI, LT							, CY, AL, TR, BG, CZ,					EE, HU, SK					
PRIORIT	Y APP	LN.	INFO	.:	LV, FI, RO, FIR,			1	US 2	002-	4273	09P	P 20021118					

WO 2003-US36880 W 20031118

OTHER SOURCE(S): MARPAT 141:17589

AB The invention provides peptide prodrugs that contain cleavage sites specifically cleaved by human kallikrein 2 (hK2). These prodrugs are useful for substantially inhibiting the nonspecific toxicity of a variable.

useful for substantially inhibiting the nonspecific toxicity of a variety of therapeutic drugs. Upon cleavage of the prodrug by hK2, the therapeutic drugs are activated and exert their toxicity. Methods for treating cell proliferative disorders are also featured in the invention.

L14 ANSWER 21 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2003:931479 CAPLUS

DOCUMENT NUMBER:

140:5049

TITLE:

Preparation of substituted 4-aryl-4H-pyrrolo[2,3-h]chromenes and analogs as activators of caspases and inducers of apoptosis and their uses against cancer

and other disorders
INVENTOR(S): Cai, Sui Xiong; Jian

Cai, Sui Xiong; Jiang, Songchun; Kemnitzer, William

E.; Zhang, Hong; Attardo, Giorgio; Denis, Real Cytovia, Inc., USA; Shire Biochem, Inc.

PATENT ASSIGNEE(S): SOURCE:

PCT Int. Appl., 110 pp.

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CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE: Patent English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	PATENT NO.						KIND DATE			APPLICATION NO.										
	WO	2003	0978	06		A2		2003	1127								0030			
	WO	2003	0978	06		А3		2004	0930											
		W:	ΑE,	AG,	AL,	ΑM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,		
			co,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,		
			GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,		
			LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NI,	NO,	NZ,	OM,		
	PH, PL, PT				PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	ТJ,	TM,	TN,	TR,	TT,		
			TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW							
		RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,		
			KG,	KZ,	MD,	RU,	TJ,	TM,	AT.	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,		
			FI,	FR,	GB,	GR,	HU,	IE,	IT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	TR,		
			BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG		
	CA	2484	702			AA		2003	1127		CA 2	003-	2484	702		2	0030	516		
	EΡ	1509	515			A2		2005	0302	1	EP 2	003-	7245	99		2	0030	516		
		R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,		
			IE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR,	BG,	CZ,	EE,	HU,	sĸ			
										0 JP 2004-506465						•				
PRIOR	PRIORITY APPLN. INFO.:							20001020			US 2002-378079P									
											WO 2						0030			

OTHER SOURCE(S): MARPAT 140:5049

The present invention is directed to substituted 4-aryl-4H-pyrrolo[2,3h]chromenes and analogs thereof (shown as I; variables defined below; e.g. II). The present invention also relates to the discovery that compds. I are activators of caspases and inducers of apoptosis. Therefore, I can be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs. The ability to activate the caspase cascade and induce apoptosis in human breast cancer cell lines T-47D and ZR-75-1 was measured for .apprx.50 examples of I, e.g. EC50 (nM) = 2.3 and 1.6, resp., for II. Although the methods of preparation are not claimed, .apprx.50 example prepns. are included. For I: R1 = alkyl, cycloalkyl, cycloalkylalkyl, hydroxyalkyl, haloalkyl, alkoxyalkyl, aminoalkyl and oxiranylalkyl; R3 and R4 = H, halo, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, C1-10 alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, nitro, amino, cyano, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, methylenedioxy, carbonylamido or alkylthio; R5 is H or C1-10 alkyl. A is (un)substituted and is aryl, heteroaryl, saturated carbocyclic, partially saturated carbocyclic, saturated heterocyclic, partially saturated heterocyclic or arylalkyl; D is (un)substituted and is a heteroarom., partially saturated (un)saturated heterocyclic fused ring, wherein said fused ring has 5 or 6 ring atoms, wherein one or two of said ring atoms are N atoms and the others of said ring atoms are C atoms. Y is CN, COR19, CO2R19 or CONR2OR21, wherein R19, R20 and R21 = H, C1-10-alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or

aminoalkyl; or R20 and R21 are taken together with the N to form a heterocycle; and Z is NR22R23, NHCOR22N(COR23)2, N(COR22)(COR23), N:CHOR19 or N:CHR19 wherein R22 and R23 = H, C1-4 alkyl or aryl, or R22 and R23 are combined together with the group attached to them to form a heterocycle.

L14 ANSWER 22 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:913055 CAPLUS

DOCUMENT NUMBER: 139:399770

TITLE: Medical goods comprising heparin or chitosan-based

hemocompatible coating

INVENTOR(S): Horres, Roland; Linssen, Marita Katharina; Hoffmann,

Michael; Faust, Volker; Hoffmann, Erika; Di Biase,

Donato

PATENT ASSIGNEE(S): Hemoteq G.m.b.H., Germany

SOURCE: PCT Int. Appl., 93 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: German FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.					KIND DATE				APPLICATION NO.						DATE		
WO.	2003	0040	an		71 20031120			WO 2003-DE1253						20030415			
NO	W:										BG,						
			•								EE,						
						•					KG,			-		-	-
											MW,	-	-	-		-	-
					_ •			,	•		SK,	•	•	•			•
								-	-	-	ZM,		,	,	,	,	,
	RW:	•	•	•	•	•	•	•	•	•	TZ,		ZM.	zw.	AM.	AZ.	BY.
	• • • • •	•	•	•			•		•	•	CH,						•
		•	•	•			•		•		NL.						
			•								GW,				-		-
DE	1022		•		Al		•				002-						
DE	1026						2004	0318	DE 2002-10261986						2	0020	510
AU	2003	2403	91		A1		2003	1111	AU 2003-240391						2	0030	415
CA	2484	269			ΑA		2003	1120	CA 2003-2484269						2	0030	415
CN	1543	362			Α	A 20041103				CN 2003-800770							
ΕP	1501	565			A1		2005	0202	EP 2003-729829						20030415		
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
		ΙE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR,	ВG,	CZ,	EE,	ΗU,	SK	
BR	2003	0114	46		Α		2005	0315		BR 2	003-	1144	6		2	0030	415
	2005						2005				003-						
	1665				Α		2005				2003-						
	2005		_				2005				2004 -						
	ZA 2004008791										2004 -				_	0041	
ZA 2004008757					Α		2005	0531			2004-				_	0041	
IORITY APPLN. INFO.:											2002-						
											002-				_		
										WO 2	2003-	DE12	53		W 2	0030	415

The invention relates to oligo- and polysaccharides containing the sugar structural element N-acylglucosamine or N-acylgalactosamine, in addition to the use thereof for producing hemocompatible surfaces and to methods for coating surfaces in a hemocompatible manner with said oligo- and polysaccharides, which constitute the common biosynthetic precursor substances of heparin, heparan sulfates and chitosan. The invention also relates to methods for producing the oligo- and/or polysaccharides, in addition to diverse application options involving hemocompatible surfaces. The invention specifically relates to the use of the oligo- and/or polysaccharides on stents involving at least one hemocompatible coating that has been applied according to the invention and that contains an anti-proliferative, anti-inflammatory and/or athrombogenic active ingredient, to methods for producing said stents and to the use of the latter for preventing restenosis. Thus desulfated and reacetylated heparin was prepared; the Ac-heparin product was used for coating coronary metal stents. The stents were implanted in swines; after four weeks the animals were anesthetized and the artery segments removed for histomorphometric anal.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 23 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:22669 CAPLUS

DOCUMENT NUMBER: 138:78473

TITLE: Oral pharmaceutical compositions with improved

bioavailability

Massironi, Maria Gabriella INVENTOR(S):

Farmatron Ltd., UK PCT Int. Appl., 19 pp. PATENT ASSIGNEE(S): SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	PATENT NO.						KIND DATE				APPLICATION NO.					DATE		
WO	2003	0021	01		A1 20030109			WO 2002-EP6748					20020619					
	W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,	
		co,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	
		GM,	HR,	ΗU,	ID,	ĮL,	IN,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,	
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NO,	ΝZ,	OM,	PH,	
		PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ΤJ,	TM,	TN,	TR,	TT,	ΤZ,	
		UA,	UG,	US,	UZ,	VN,	ΥU,	ZA,	ZM,	Z₩								
	RW:	GH,	GM,	ΚE,	LS,	MW,	ΜZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	ΑT,	BE,	CH,	
		CY,	DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PΤ,	SE,	TR,	
		BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG	
CA	24513	377			AA		2003	0109		CA 2	2002-	2451	377		2	0020	619	
EP	1401	405			A1		2004	0331		EP 2	2002-	7547	06		2	0020	619	
EP	1401	405			В1		2005	0831										
•	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,	
		ΙE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR							
JP	2004	53483	32		Т2		2004	1118		JP 2	2003-	5083	40		2	0020	619	
AT	30313	37			E		2005	0915		AT 2	2002-	7547	06		2	0020	619	
PT	1401	405			Т		2005	1130		PT 2	2002-	7547	06		2	0020	619	
US	20042	24766	56		A1		2004	1209	1	US 2	2004-	4824	60		2	0040	723	
PRIORITY	APP	LN.	INFO	. :						IT 2	2001-1	MI13	38	7	A 2	0010	626	
									1	WO 2	2002-	EP67	48	1	N 2	0020	619	

AB The present invention relates to prompt-release oral pharmaceutical compns. containing 1 or more drugs solubilized, suspended or embedded in a suitably formulated amphiphilic matrix for improving in vitro and in vivo bioavailability of medicaments sparingly absorbed through the oral route and/or with problems of high variability of absorption in the gastrointestinal tract. Gelucire 44/14 (500 g) is melted at 55-65°, and the molten mass is added under stirring to 50 g etoposide to obtain a homogeneous solution/dispersion. The resulting mixture is added in succession under stirring to 5 g sodium lauryl sulfate and 45 g  $\beta-$  cyclodextrin. The resulting mixture is stirred for at least 15 min at 55°, and then hard-gelatin capsules are filled with a distributing syringe, to reach a 600-mg capsule. Each capsule is then closed and sealed by spraying with 50% ethanol and water and subsequent heating under hot air to obtain the final capsule. The resulting capsules have in vitro release not <80% after 30 min.

L14 ANSWER 24 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:888735 CAPLUS

DOCUMENT NUMBER: 137:369971

TITLE: Preparation of substituted 4H-chromenes and analogs as activators of caspases and inducers of apoptosis and

their uses against cancer and other disorders

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

INVENTOR(S): Cai, Sui Xiong; Zhang, Hong; Jiang, Songchun; Storer,

Richard

PATENT ASSIGNEE(S):

Cytovia, Inc., USA PCT Int. Appl., 139 pp. SOURCE:

CODEN: PIXXD2 Patent

DOCUMENT TYPE: LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

REFERENCE COUNT:

PATENT NO	KINI	)	DATE		APPLICATION NO.						DATE					
WO 2002092594 WO 2002092594				A1 C1		20021121 20040624		WO 2002-US15399						20020516		
₩: A C C		AG, CR, IR, T,	AL, CU, HU, LU,	AM, CZ, ID, LV,	AT, DE, IL, MA,	AU, DK, IN, MD,	AZ, DM, IS, MG,	DZ, JP, MK,	EC, KE, MN,	EE, KG, MW,	ES, KP, MX,	FI, KR, MZ,	GB, KZ, NO,	GD, LC, NZ,	GE, LK, OM,	GH, LR, PH,

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UA, UG, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
              KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
              GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2447010
                            AΑ
                                    20021121
                                                 CA 2002-2447010
                                                                           20020516
     US 2003065018
                                    20030403
                                                 US 2002-146138
                            A1
                                                                           20020516
     EP 1392683
                            A1
                                   20040303
                                                 EP 2002-741704
                                                                           20020516
          R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
                                    20040728
                                                 CN 2002-812067
     CN 1516700
                                                                           20020516
                             Α
     JP 2004530692
                             Т2
                                    20041007
                                                 JP 2002-589478
                                                                           20020516
     US 2006035925
                             A1
                                    20060216
                                                 US 2005-150586
                                                                           20050613
                                                 US 2001-290997P
PRIORITY APPLN. INFO.:
                                                                          20010516
                                                 US 1999-163584P
                                                                        P 19991105
                                                                        P 20000224
                                                 US 2000-185211P
                                                 US 2000-705840
                                                                        A2 20001106
                                                 US 2002-146138
                                                                        Al 20020516
                                                 WO 2002-US15399
                                                                        W 20020516
OTHER SOURCE(S):
                           MARPAT 137:369971
     The present invention is directed to substituted 4H-chromenes and analogs
     thereof (shown as I; e.g. 2-amino-3-cyano-7-hydroxy-4-(3-bromo-4,5-
     dimethoxyphenyl)-4H-chromene). It also relates to the discovery that I
     are activators of caspases and inducers of apoptosis and, therefore, can
     be used to induce cell death in a variety of clin. conditions in which
     controlled growth and spread of abnormal cells occurs. In I: R1-R4 = H,
     halo, haloalkyl, aryl, fused aryl, carbocyclic, heterocyclic, heteroaryl,
     Cl-10 alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl,
     heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, nitro, amino,
     cyano, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy,
     methylenedioxy, carbonylamido or alkylthio; or R1 and R2, or R2 and R3, or
     R3 and R4, taken together with the atoms to which they are attached form
     an aryl, heteroaryl, partially saturated carbocyclic or partially saturated heterocyclic group, wherein said group is optionally substituted. R5 is H
     or C1-10 alkyl; A is optionally substituted and is aryl, heteroaryl, saturated
     carbocyclic, partially saturated carbocyclic, saturated heterocyclic, partially saturated heterocyclic or arylalkyl; Y is CN, COR7, CO2R7 or CONRxRy, wherein
     R7, Rx and Ry = H, C1-10 alkyl, haloalkyl, aryl, fused aryl, carbocyclic,
     heterocyclic, heteroaryl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkynyl, heteroarylalkynyl,
     carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl; or Rx and
     Ry are taken together with the N to which they are attached to form a
     heterocycle; and Z is NR8R9, NHCOR8, N(COR9)2, N(COR8)(COR9), N:CHOR8 or
     N:CHR8, wherein R8 and R9 = H, Cl-4 alkyl or aryl, or R8 and R9 are
     combined together with the group attached to them to form a heterocycle.
     The EC50 values for >80 I against T-47D and ZR-75-1 human breast cancer
     cell lines are tabulated, e.g. 30 and 25 nM, resp., for
     2-amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-indolo[7,6-b]pyran.
     Although the methods of preparation are not claimed, 81 example prepns. are
     included.
REFERENCE COUNT:
                                   THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS
                                   RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L14 ANSWER 25 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:
                            2002:408471 CAPLUS
DOCUMENT NUMBER:
                            136:406862
TITLE:
                            Polymer-based oral nanosphere delivery systems
INVENTOR(S):
                            Dunn, James M.
PATENT ASSIGNEE(S):
                            PR Pharmaceuticals, Inc., USA
SOURCE:
                            PCT Int. Appl., 34 pp.
                            CODEN: PIXXD2
DOCUMENT TYPE:
                            Patent
LANGUAGE:
                            English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                                                 APPLICATION NO.
                                                                           DATE
                            KIND
                                    DATE
                            ----
     WO 2002041829
                             A2
                                    20020530
                                                 WO 2001-US43299
                                                                           20011120
     WO 2002041829
                             А3
                                    20020718
          W: AU, CA, JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
              PT, SE, TR
     CA 2429254
                                    20020530
                                                 CA 2001-2429254
                                                                            20011120
                             AA
     AU 2002039279
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AU 2002-39279

20011120

A5

20020603

PRIORITY APPLN. INFO.: US 2000-252070P P 20001120 WO 2001-US43299 W 20011120 Oral nanoparticulate pharmaceutical formulations and related methods for

controlled release delivery of chemotherapeutic and macromol. agents are described. A nanoparticulate formulation comprises a therapeutic agent, e.g., heparin or insulin, and a structural delivery component, a polymer, e.g., a lactide-glycolide copolymer, in an amount sufficient to achieve a therapeutic plasma concentration and sustain the concentration over time. The formulation may further include  $\beta$ - cyclodextrin, polyvinyl alc., and a bioadhesive adjuvant. For example, heparin nanospheres were formed from 1:1 (weight/weight) poly(DL-lactide-co-glycolide) and heparin with the emulsion prepared in an aqueous solution of  $\beta$ -  ${ t cyclodextrin}$  and polyvinyl alc. Doses of 200, 400, and 600 mg/kg were administered by oral gavage in aqueous bioadhesive polymer adjuvant solution to rabbits. The ability to achieve significant heparin plasma levels by 2 h post dosing, and to sustain levels to 10 days was illustrated. Also, an improved insulin nanosphere formulation was prepared using Eudragit RS 30 1000 mg, Phospholipon 90H 500 mg, β- cyclodextrin 1000 mg, insulin powder 50 mg, and ethanol 50 mL. The formulation showed improved suppression of glucose levels in diabetic rats and extension of the effect to at least 96 h. Nanospheres may be incorporated into a tablet preparation

L14 ANSWER 26 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN ACCESSION NUMBER: 1998:716914 CAPLUS

ACCESSION NUMBER:

DOCUMENT NUMBER: 130:9142

TITLE: More space-group corrections: from triclinic to centered monoclinic and to rhombohedral: also from P1

to P.hivin.1 and from Cc to C2/c

AUTHOR(S): Herbstein, Frank H.; Marsh, Richard E.

Department of Chemistry, Technion-Israel Institute Technology, Haifa, 32000, Israel CORPORATE SOURCE:

Acta Crystallographica, Section B: Structural Science SOURCE:

(1998), B54(5), 677-686 CODEN: ASBSDK; ISSN: 0108-7681

Munksquard International Publishers Ltd. PUBLISHER:

DOCUMENT TYPE: Journal

LANGUAGE: English

The authors present 14 examples of crystal structures that were originally described as triclinic, but are properly described as either C-centered monoclinic (ten examples) or rhombohedral (four examples). There is also one example each of changes from P1 to P.hivin.1 and from Cc to C2/c.

THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 46 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 27 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

1998:133475 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 128:145378

TITLE: Inhibitor of tumor metastasis or recurrence

INVENTOR(S): Sudo, Katsuichi; Houkan, Takashi

PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan

Eur. Pat. Appl., 17 pp. SOURCE:

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	ENT 1	NO.			KINI	)	DATE		AP	PLICAT	I NOI	NO.		D <i>I</i>	ATE		
						-											
EΡ	81943	30			A1		1998	0121	EP	1997-	-3053	48		19	970	717	
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB, G	R, IT,	LI,	LU,	NL,	SE,	PT,	ΙE,	FΙ
CA	2210	600			AA		1998	0117	CA	1997-	-2210	600		19	970	716	
JP	1008	1631			A2		1998	0331	JP	1997-	-1912	20		19	970	716	
ORITY	( APP	LN.	INFO	.:					JP	1996-	-1878	31	P	19	960	717	
		. ~ .				~~~											

OTHER SOURCE(S): MARPAT 128:145378

A pharmaceutical composition comprising an angiogenesis inhibitor such as a fumagillol derivative is used for inhibition of tumor metastasis or recurrence. A solution was prepared containing 6-0-(N-

chloroacetylcarbamoyl)fumagillol (I) 100, maltosyl-βcyclodextrin 726 mg, NaOH 33.3  $\mu$ g, and distilled water for

injection to 5.0mL. I was shown to enhance or potentiated the antitumor activity of other antitumor agents such as cisplatin.

THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 8 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

1994:621209 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 121:221209

TITLE: Potentiation of cytotoxic cancer therapies by TNP-470

alone and with other anti-angiogenic agents

Teicher, Beverly A.; Holden, Sylvia A.; Ara, Gulshan; AUTHOR(S):

Alvarez Sotomayor, Enrique; Huang, Zhen Dong; Chen,

Ying Nan; Brem, Harold

CORPORATE SOURCE: Dana-Farber Cancer Institute, Boston, MA, 02115, USA International Journal of Cancer (1994), 57(6), 920-5 SOURCE:

CODEN: IJCNAW; ISSN: 0020-7136

DOCUMENT TYPE: Journal LANGUAGE: English

The ability of TNP-470, a synthetic analog of fumagillin which has been AB described as an anti-angiogenic agent, to potentiate cytotoxic cancer therapies was investigated in vivo in the murine FSaIIC fibrosarcoma and the Lewis lung carcinoma. TNP-470 was more toxic toward FSaIIC tumor cells from tumors treated in vivo than toward bone-marrow CFU-GM from the same animals. TNP-470 had a dose-modifying effect on the toxicity of cyclophosphamide toward FSaIIC tumor cells which amounted to an 8-fold increase in tumor-cell killing at a cyclophosphamide dose of 500 mg/kg. Treatment with TNP-470 and minocycline increased the permeability of the FSaII fibrosarcoma in vivo to the fluorescent dye Hoechst 33342 and increased the killing of both the bright and the dim tumor cells by **cyclophosphamide**. TNP-470, especially in combination with minocycline, formed a highly effective modulator combination for treatment of the Lewis lung carcinoma with cytotoxic cancer therapies against primary and metastatic disease. The combination of TNP-470/minocycline and cyclophosphamide led to 40 to 50% long-term survivors in Lewis-lung-carcinoma-bearing animals. Our results indicate that the use of anti-angiogenic modulators in cancer therapy is a very promising area for further study.

L14 ANSWER 29 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

1994:203216 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 120:203216

TITLE: Collection of enantiomer separation factors obtained

by capillary gas chromatography on chiral stationary

phases Anon.

AUTHOR(S): CORPORATE SOURCE: Germany

Journal of High Resolution Chromatography (1993), SOURCE:

16(6), 338-52 CODEN: JHRCE7; ISSN: 0935-6304

DOCUMENT TYPE: Journal LANGUAGE: English

The separation factors obtained by capillary gas chromatog. on heptakis(2,6-di-O-methyl-3-O-pentyl)- $\beta$ - cyclodextrin chiral

stationary phases are given for many enantiomers.

L14 ANSWER 30 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

1994:69602 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 120:69602

TITLE: Preparation and use of polyanionic polymer-based conjugates targeted to vascular endothelial cells

INVENTOR(S): Thorpe, Philip E.

PATENT ASSIGNEE(S): University of Texas System, USA; Imperial Cancer

Research Technology Ltd.

SOURCE: PCT Int. Appl., 117 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	PATENT NO.				KIND DATE				APPLICATION NO. DATE
WO	9318	 793			A1	-	1993	 0930	WO 1993-US2619 19930322
	W:	AT,	ΑU,	BB,	BG,	BR,	CA,	CH,	CZ, DE, DK, ES, FI, GB, HU, KP, KR,
		LU,	MG,	MN,	MW,	NL,	NO,	PL,	PT, US
	RW:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB, IE, IT, LU, MC, NL, PT, SE, BF,
		ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	ML, MR
US	5474	765			Α		1995	1212	US 1992-856018 19920323
ΑU	9338	166			A1		1993	1021	AU 1993-38166 19930322
EΡ	6327	28			A1		1995	0111	EP 1993-907633 19930322
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB, GR, IE, IT, LI, LU, MC, NL, PT
US	5762	918			Α		1998	0609	US 1994-307745 19941205

PRIORITY APPLN. INFO.:

US 1992-856018 A2 19920323 WO 1993-US2619 A 19930322

An anionic polymer (e.g. a heparin derivative) is linked to an active agent (especially a steroid), preferably by a selectively hydrolyzable bond, for delivery of the active agent to vascular endothelial cells. The conjugates are useful as angiogenesis inhibitors for treatment of e.g. cancer, arthritis, and diabetic blindness. Thus, heparin was condensed with adipic dihydrazide and then with cortisol; the cortisol:heparin mol ratio in the product was 8-9. This conjugate was markedly acid labile, suppressed DNA synthesis and cell migration in human umbilical vein endothelial cells, retarded or abolished the vascularization of sponges in vivo, and retarded lung tumor growth in mice by 65%. No adverse effects of the conjugate were detected, and equivalent treatments with a mixture of heparin and cortisol were significantly less effective in all cases.

L14 ANSWER 31 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:658220 CAPLUS

DOCUMENT NUMBER:

117:258220

TITLE:

A composition containing a tetracycline for inhibiting

angiogenesis

INVENTOR(S):

Brem, Henry; Tamargo, Rafael J.; Bok, Robert A.

PATENT ASSIGNEE(S):

SOURCE:

PCT Int. Appl., 24 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9212717	A2	19920806	WO 1992-US254	19920115
WO 9212717	A3	19921015		
W: AU, CA, JP,	KR, US			
RW: AT, BE, CH,	DE, DK	, ES, FR, GB	, GR, IT, LU, MC, NL,	SE
AU 9214119	A1	19920827	AU 1992-14119	19920115
US 6482810	B1	20021119	US 1994-227100	19940413
PRIORITY APPLN. INFO.:			US 1991-641498	A2 19910115
			WO 1992-US254	A 19920115

AB Pharmaceuticals containing tetracycline and other drugs are useful for the inhibition of angiogenesis. The drugs can be delivered topically, locally or systemically and are extremely selective for growth of endothelial cells. Thus, minocycline and heparin and cortisone acetate were incorporated into the ethylene-vinyl acetate copolymer matrix and the inhibition of angiogenesis in the rabbit cornea was evaluated. Tumor angiogenesis was inhibited by the controlled release of minocycline, and cortisone and heparin.

L17 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:78792 CAPLUS

DOCUMENT NUMBER: 142:297785

Study of the Michael addition of  $\beta$ -TITLE:

cyclodextrin-thiol complexes to conjugated

alkenes in water

Krishnaveni, N. Srilakshmi; Surendra, K.; Rao, K. Rama AUTHOR (S): CORPORATE SOURCE:

Organic Chemistry Division-I, Indian Institute of

Chemical Technology, Hyderabad, 500 007, India Chemical Communications (Cambridge, United Kingdom)

(2005), (5), 669-671 CODEN: CHCOFS; ISSN: 1359-7345

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 142:297785

An environmentally benign and highly efficient supramol. Michael addition of

thiols from the secondary side of β- cyclodextrin to

 $\alpha,\beta$ -unsatd. compds. at the primary side in water is described. Products of undesirable side reactions resulting from polymerization were not

observed; the use of cyclodextrin precluded the use of either acid

or base and the catalyst can be recovered and reused.

REFERENCE COUNT: THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS 49 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:787673 CAPLUS

DOCUMENT NUMBER: 142:148242

TITLE: Inhibition of brush border dipeptidase with cilastatin

reduces toxic accumulation of cyclosporin A in kidney

proximal tubule epithelial cells

AUTHOR (S): Perez, Maria; Castilla, Manuela; Torres, Ana Maria;

Lazaro, Jose Antonio; Sarmiento, Elisabeth; Tejedor,

Alberto

CORPORATE SOURCE: Department of Nephrology, Hosp. Gen. Univ. Gregorio

Maranon, Madrid, Spain

SOURCE: Nephrology, Dialysis, Transplantation (2004), 19(10),

2445-2455

CODEN: NDTREA; ISSN: 0931-0509

PUBLISHER: Oxford University Press DOCUMENT TYPE: Journal

LANGUAGE: English

Cilastatin reduces nephrotoxicity associated with cyclosporin A (CyA) in solid organ and bone marrow transplantation. This appears to be unrelated to changes in renal hemodynamics or CyA metabolism How cilastatin induces this protection is unclear, but it could result from changes on accumulation of CyA proximal cells. We investigated the effects of cilastatin on primary cultures of pig kidney proximal tubule epithelial cells (PTECs) treated with CyA and FK506. Cell membrane fluidity and membrane-bound cholesterol-rich raft (MBCR) distribution were evaluated by fluorescence microscopy, and CyA transport by RIA. Changes in CyA- and FK506-induced apoptosis were also evaluated by electron and light microscopy, flow cytometry, and detection of cytoplasmic nucleosomes by ELISA. CyA caused a dose-dependent reduction of cell membrane fluidity, which was prevented by pre-treating PTECs with cilastatin. Cilastatin also inhibited CyA transport across membranes and reduced recovery of CyA in mitochondria and membrane-bound fractions from cilastatin-treated PTECs. This effect was not related to an altered distribution of MBCRs, which are essential for CyA transport. Cilastatin protected against CyA- and FK506-induced apoptosis. Prevention of CyA-induced reduction of cell membrane fluidity and inhibition of CyA transport are features of cilastatin's direct effects on PTECs. Unaltered distribution of MBCRs in the presence of cilastatin suggests that cilastatin binding to raft-bound dipeptidases, rather than MBCR modifications, causes interference with CyA transport. These results provide addnl. insight into the mechanisms and scope of cilastatin nephroprotection.

REFERENCE COUNT: THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS 20 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:298522 CAPLUS

DOCUMENT NUMBER: 137:93916

TITLE: Inclusion complexation thermodynamics of acridine red

and rhodamine B by natural and novel

oligo(ethylenediamine) tethered Schiff base β-

cyclodextrin

AUTHOR (S): Liu, Yu; Jin, Lan; Zhang, Heng-Yi CORPORATE SOURCE: Department of Chemistry, Nankai University, Tianjin,

300071, Peop. Rep. China

Journal of Inclusion Phenomena and Macrocyclic SOURCE:

Chemistry (2002), 42(1-2), 115-120 CODEN: JIPCF5; ISSN: 1388-3127

PUBLISHER: Kluwer Academic Publishers

DOCUMENT TYPE: Journal LANGUAGE: English

A series of Schiff base  $\beta$ - cyclodextrin derivs. with an oligo(ethylenediamine) tether have been newly synthesized and their inclusion complexation behavior has been assessed and discussed thermodynamically, employing acridine red (AR) and rhodamine B (RhB) as representative guests. Fluorescence spectrophotometric titrns. have been performed in methanol-water (1: 2) phosphate buffer solution (pH = 7.20) at 25.0-45.0 °C in order to obtain the complex stability consts. (KS)

and the thermodn. parameters ( $\Delta H^{\circ}$  and  $T\Delta S^{\circ}$ ) for the stoichiometric 1: 1 inclusion complexation of two guests with the native and modified  $\beta$ - cyclodextrins. As compared with the parent  $\beta$ - cyclodextrin, all of the chemical modifications to

the primary side of  $\beta$ - cyclodextrins examined led to substantial decreases for rhodamine B and marked increases for acridine red in complex stability, which are elucidated in terms of the induced-fit interaction and the complementary geometrical relationship between the host  $\beta$ - cyclodextrins and guest mols., as well as the length of the linking chain of  $\beta$ -CD derivs. The induced CD spectral analyses of these  $\beta$ - cyclodextrin derivs. indicated that the aromatic moiety in modified  $\beta$ - cyclodextrins is not embedded into the hydrophobic cavity of cyclodextrin. The inclusion complexation with acridine red possess higher binding consts. than that

with rhodamine B, which are solely attributed to the increased enthalpic gain. Thermodynamically, the inclusion complexation with the modified  $\beta$ - cyclodextrins is absolutely enthalpy-driven for acridine

red, while for complexation with rhodamine B is mainly entropy-driven. REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 4 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

DUPLICATE 1

ACCESSION NUMBER: 2001:436303 BIOSIS DOCUMENT NUMBER: PREV200100436303

TITLE: Alternative methodologies for the determination of

aldehydes by capillary electrophoresis.

AUTHOR (S): Pereira, Elisabete Alves; Tavares, Marina Franco Maggi

[Reprint author]; Cardoso, Arnaldo Alves Universidade de Sao Paulo, Instituto de Quimica, 05599-970, CORPORATE SOURCE:

Sao Paulo, SP, Brazil

SOURCE: Journal of AOAC International, (November-December, 1999)

Vol. 82, No. 6, pp. 1562-1570. print.

ISSN: 1060-3271.

DOCUMENT TYPE: Article LANGUAGE: English

ENTRY DATE: Entered STN: 12 Sep 2001

Last Updated on STN: 22 Feb 2002

This paper describes 2 alternative methodologies for the determination of selected aldehydes (formaldehyde, acetaldehyde, propionaldehyde, acrolein, and benzaldehyde) by capillary electrophoresis (CE). The first approach is based on the formation of aldehyde-bisulfite adducts and employs free solution CE with reversed electroosmotic flow and indirect detection, using 10 mmol/L 3,5-dinitrobenzoic acid (pH 4.5) containing 0.2 mmol/L cetyltrimethylammonium bromide as the electrolyte. This novel methodology showed a fairly good sensitivity to concentration, with detection limits with respect to a single aldehyde on the order of 10-40 mug/L, a reasonable analysis time (separation was achieved in <8 min), and no need for sample manipulation. A second approach was proposed in which 2,4-dinitrophenylhydrazine derivatives of the aldehydes were detected in a micellar electrolyte medium (20 mmol/L borate buffer containing 50 mmol/L sodium dodecyl sulfate and 15 mmol/L betacyclodextrin). This latter methodology included a laborious
sample preconcentration step and showed much poorer sensitivity (0.5-2 mg/L detection limit, with respect to a single aldehyde), despite the use of sodium chloride to promote sample stacking. Both methodologies proved adequate to evaluate aldehyde levels in vehicular emissions. Samples from the tailpipe exhaust of a passenger car vehicle without a catalytic converter and operated with an ethanol-based fuel were collected and analyzed; the results showed high levels of formaldehyde and acetaldehyde  $(0.41-6.1\ ppm,\ v/v)$ . The concentrations estimated by the 2 methodologies, which were not in good agreement, suggest the possibility of striking differences in sample collection efficiency, which was not the concern of

this work.

L17 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:229290 CAPLUS

DOCUMENT NUMBER: 114:229290

TITLE: Chiral reaction medium for organic reactions
INVENTOR(S): Lubineau, Andre; Bienayme, Hugues; Queneau, Yves

PATENT ASSIGNEE(S): Beghin-Say S. A., Fr. SOURCE: PCT Int. Appl., 20 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: French

LANGUAGE: Fren FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA.	TENT NO.		KIND	DATE	APPLICATION NO.		DATE	
WO	9012773		A1	19901101	WO 1990-FR267		19900412	
	W: JP,	US						
	RW: AT,	BE, C	I, DE, I	DK, ES, FR,	GB, IT, LU, NL, SE			
FR	2645855		A1	19901019	FR 1989-4950		19890414	
FR	2645855		B1	19910920				
EP	423300		A1	19910424	EP 1990-907136		19900412	
EP	423300		B1	19950104				
	R: AT,	BE, CI	i, DE, 1	DK, ES, FR,	GB, IT, LI, LU, NL,	SE		
JP	03505743		T2	19911212	JP 1990-506957		19900412	
US	5169943		Α	19921208	US 1990-623707		19901214	
PRIORITY	APPLN.	INFO.:			FR 1989-4950	A	19890414	
					WO 1990-FR267	W	19900412	

AB Chiral reaction media containing mono-, di-, or trisaccharides increase the reaction rate of Diels-Alder reactions. In the Diels-Alder reaction of 1-( $\beta$ -D-glucosyloxy)-1,3-butadiene with CH2:CHCOMe, a reaction medium of 2M glucose showed a reaction rate constant (k+105M-1s-1) of 44.6 compared with 28.2 for H2O alone. Other additives were ribose, galactose, saccharose,  $\beta$ - cyclodextrin, mannose, and Me  $\alpha$ -glucoside.